

Contents

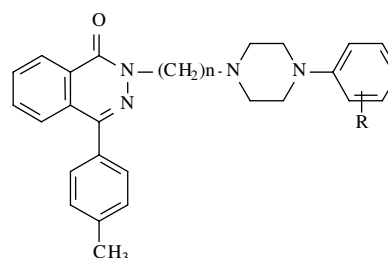
ARTICLES

New 4-(4-methyl-phenyl)phthalazin-1(2*H*)-one derivatives and their effects on α_1 -receptors

pp 2575–2579

Giovannella Strappaghetti,* Chiara Brodi, Gino Giannaccini and Laura Betti

Continuing our research aimed at obtaining new compounds with high affinity and selectivity toward α_1 -AR, a new class of arylpiperazine derivatives has been synthesized. The new compounds are characterized by a 4-methyl-phenyl-phthalazinone system linked, through a linker of two-, four- or seven-carbon atoms, to an arylpiperazine moiety. The pharmacological profile of these compounds was evaluated for their affinities toward α_1 - and α_2 -AR, and toward 5HT_{1A} receptor. A discussion on the structure–activity relationship of such compounds is also reported.



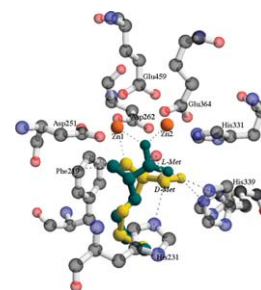
n = 2,4,7;
R = H;
R = *o*-OCH₃;
R = *o*-OC₂H₅;
R = *o*-CH(CH₃)₂;
R = *m*-CF₃;
R = *m*-Cl.

Human methionine aminopeptidase type 2 in complex with L- and D-methionine

pp 2580–2583

M. Cristina Nonato, Joanne Widom and Jon Clardy*

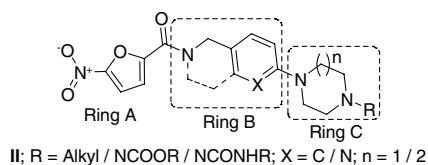
The crystal structures of human type 2 methionine aminopeptidase complexed with L- and D-methionine were deduced by X-ray crystallography to establish the structural basis of enantiomer discrimination in natural substrates and inhibitors.



Synthesis of new and potent analogues of anti-tuberculosis agent 5-nitro-furan-2-carboxylic acid 4-(4-benzyl-piperazin-1-yl)-benzylamide with improved bioavailability

pp 2584–2589

Rajendra P. Tangallapally, Robin E. B. Lee, Anne J. M. Lenaerts and Richard E. Lee*

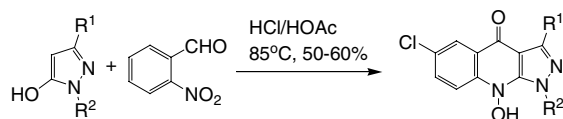


The synthesis of lead optimized analogues, their anti-tuberculosis activity, and bioavailability are reported.

Synthesis and SAR of 1,9-dihydro-9-hydroxypyrazolo[3,4-*b*]quinolin-4-ones as novel, selective c-Jun N-terminal kinase inhibitors

pp 2590–2594

Mei Liu,* Zhili Xin, Jill E. Clampit, Sanyi Wang, Rebecca J. Gum, Deanna L. Haasch, James M. Trevillyan, Cele Abad-Zapatero, Elizabeth H. Fry, Hing L. Sham and Gang Liu



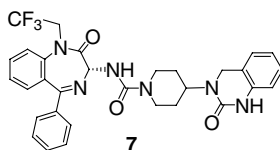
This paper describes a novel class of 1,9-dihydro-9-hydroxypyrazolo[3,4-*b*]quinolin-4-ones as c-Jun-N-terminal kinase (JNK) inhibitors. These compounds were synthesized via the condensation of 2-nitrobenzaldehydes and hydroxypyrazoles. The structure–activity relationships (SARs) and kinase selectivity profile of the inhibitors are also discussed. Compound **16** was identified as a potent JNK inhibitor with good cellular potency.



Non-peptide calcitonin gene-related peptide receptor antagonists from a benzodiazepinone lead

pp 2595–2598

Theresa M. Williams,* Craig A. Stump, Diem N. Nguyen, Amy G. Quigley, Ian M. Bell, Steven N. Gallicchio, C. Blair Zartman, Bang-Lin Wan, Kimberly Della Penna, Priya Kunapuli, Stefanie A. Kane, Ken S. Koblan, Scott D. Mosser, Ruth Z. Rutledge, Christopher Salvatore, John F. Fay, Joseph P. Vacca and Samuel L. Graham

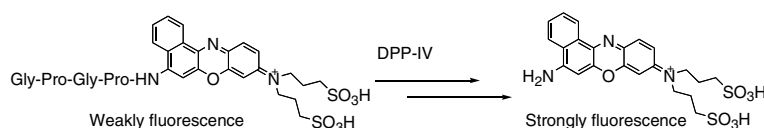


Structure activity studies led to the non-peptide CGRP antagonist, **7** ($K_i = 44$ nM, $IC_{50} = 38$ nM), which was orally bioavailable in rats. Benzodiazepinone **7** is a promising new lead in the development of orally bioavailable CGRP antagonists for the treatment of migraine.

Development of a dual fluorogenic and chromogenic dipeptidyl peptidase IV substrate

pp 2599–2602

Nan-Hui Ho, Ralph Weissleder and Ching-Hsuan Tung*

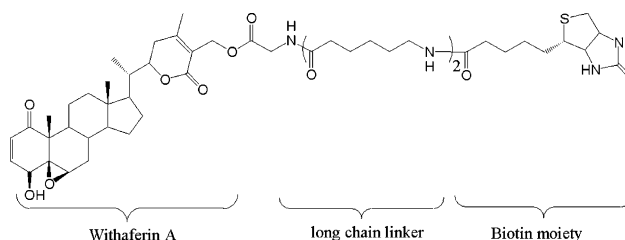


A water-soluble far-red tetrapeptide substrate was developed to sense DPP-IV activity.

Development of withaferin A analogs as probes of angiogenesis

pp 2603–2607

Yasuno Yokota, Paola Bargagna-Mohan, Padma P. Ravindranath, Kyung B. Kim and Royce Mohan*

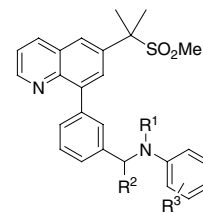


Nitrogen-bridged substituted 8-arylquinolines as potent PDE IV inhibitors

pp 2608–2612

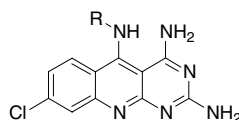
Patrick Lacombe,* Denis Deschênes, Daniel Dubé, Laurence Dubé, Michel Gallant, Dwight Macdonald, Antony Mastracchio, Hélène Perrier, Stella Charleson, Zheng Huang, France Laliberté, Susana Liu, Joseph A. Mancini, Paul Masson, Myriam Salem, Angela Styhler and Yves Girard

Potent inhibitors of the human PDE IV enzyme are described. Substituted 8-arylquinoline analogs bearing nitrogen-linked side chain were identified as potent inhibitors based on the SAR described herein.

**Docking studies and development of novel 5-heteroaryl-amino-2,4-diamino-8-chloropyrimido-[4,5-*b*]quinolines as potential antimalarials**

pp 2613–2617

Advait A. Joshi and C. L. Viswanathan*

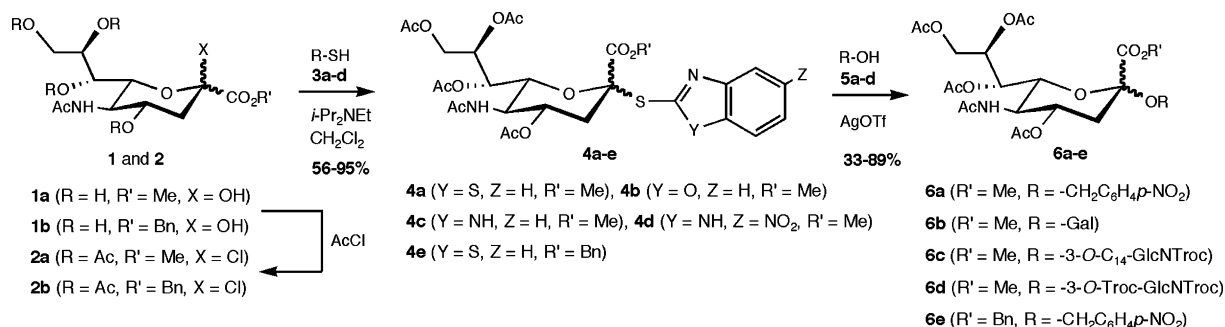


Docking is used to predict the binding mode of novel 5-substituted amino-2,4-diamino-8-chloropyrimido-[4,5-*b*]quinolines and to design and synthesize three novel analogs.

Novel glycosylation reactions using glycosyl thioimidates of *N*-acetylneuraminic acid as sialyl donors

pp 2618–2620

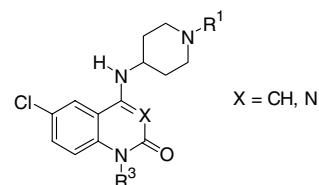
Kiyoshi Ikeda,* Misato Aizawa, Kazuki Sato and Masayuki Sato

**Identification and characterization of amino-piperidinequinolones and quinazolinones as MCHr1 antagonists**

pp 2621–2627

Christopher Blackburn,* Matthew J. LaMarche, James Brown, Jennifer Lee Che, Courtney A. Cullis, Sujen Lai, Martin Maguire, Thomas Marsilje, Bradley Geddes, Elizabeth Govek, Vivek Kadambi, Colleen Doherty, Brian Dayton, Sevan Brodjian, Kennan C. Marsh, Christine A. Collins and Philip R. Kym

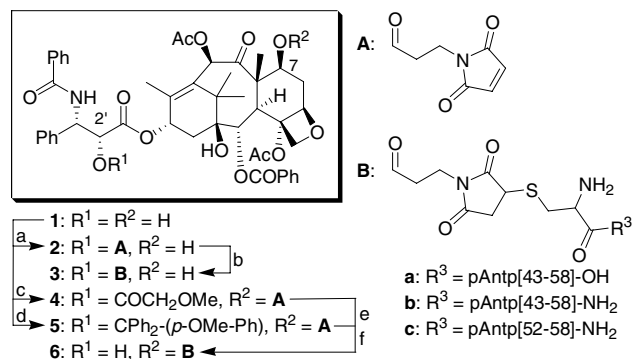
Several potent, functionally active MCHr1 antagonists derived from quinolin-2(1*H*)-ones and quinazolin-2(1*H*)-ones have been synthesized and evaluated. Pyridylmethyl substitution at the quinolone 1-position results in derivatives with low-nM binding potency and good selectivity with respect to hERG binding.



Synthesis and biological activity of conjugates between paclitaxel and the cell delivery vector penetratin

Shudong Wang,* Nikolai Z. Zhelev, Susan Duff and Peter M. Fischer

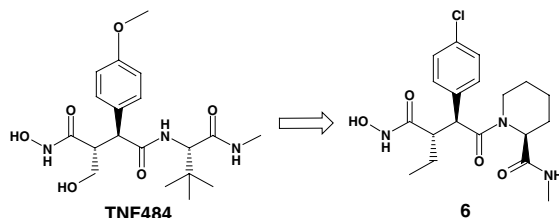
Synthesis of paclitaxel–penetratin (pAntp) constructs, in which the 2'- or 7-position of paclitaxel was used as the attachment site for linkers connecting the drug and peptide moieties, is described. Conjugates **3b** and **3c** were highly soluble and stable with a half-life of >8 h under cell culture conditions. Their antitumour activities were determined.



A cassette-dosing approach for improvement of oral bioavailability of dual TACE/MMP inhibitors

Philipp Janser,* Ulf Neumann, Wolfgang Miltz, Roland Feifel and Thomas Buhl

pp 2632–2636



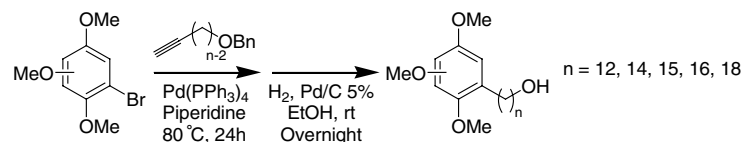
Tenfold improvement of the oral bioavailability of TNF484 with the help of cassette-dosing is described.



Quinol fatty alcohols as promoters of axonal growth

Mazen Hanbali, Marta Vela-Ruiz, Dominique Bagnard and Bang Luu*

pp 2637–2640

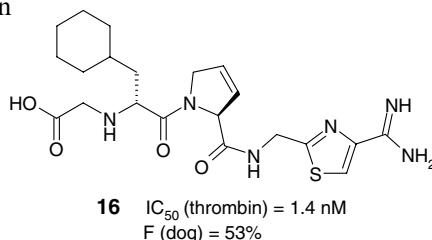


Three series of quinol fatty alcohols were synthesized and their capacity to promote axonal growth was evaluated. Q₂FA15, bearing 15 carbon atoms on the side chain, exhibits the highest promoting effect (10⁻⁹ M) allowing axonal growth on both permissive and non-permissive (glial scar) environments.

Orally active thrombin inhibitors. Part 1: Optimization of the P1-moiety

Helmut Mack,* Dorit Baucke, Wilfried Hornberger, Udo E. W. Lange,* Werner Seitz and H. Wolfgang Höffken

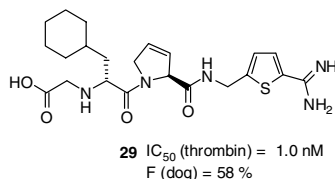
pp 2641–2647



Highly potent thrombin inhibitors and their SAR with focus on the P1-position are described. The aryl P1-moiety mimicking the Arg part of the (D)-Phe-Pro-Arg derived thrombin inhibitors turned out to be a key component for in vitro potency and in vivo activity.

Orally active thrombin inhibitors. Part 2: Optimization of the P2-moiety

pp 2648–2653

Udo E. W. Lange,* Dorit Baucke, Wilfried Hornberger, Helmut Mack,*
Werner Seitz and H. Wolfgang Höffken

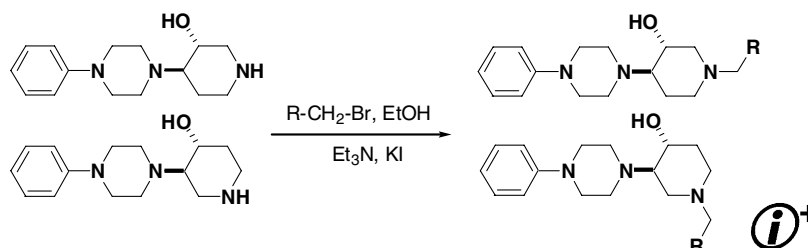
The convergent synthesis of highly potent thrombin inhibitors and their SAR with focus on the P2-position is described. The special 'dehydroproline' effect on the in vitro potency and in vivo activity is discussed for selected examples.

Synthesis and in vitro evaluation of N-substituted aza-trozamicol analogs as vesicular acetylcholine transporter ligands

pp 2654–2657

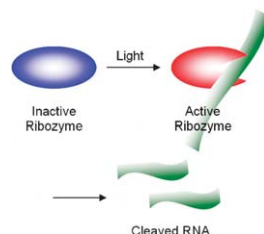
Thaer Assaad, Sylvie Mavel, Stanley M. Parsons, Shane Kruse, Laurent Galineau, Hassan Allouchi,
Michael Kassiou, Sylvie Chalon, Denis Guilloteau and Patrick Emond*

Aza-trozamicol derivatives substituted at the nitrogen of the piperidine ring with alkyl, alk-2-enyl or benzyl groups were synthesized. The N-substitution with *ortho* or *meta* bromobenzyl groups gave compounds with high affinity for human VACHT.

**Photochemical hammerhead ribozyme activation**

pp 2658–2661

Douglas D. Young and Alexander Deiters*

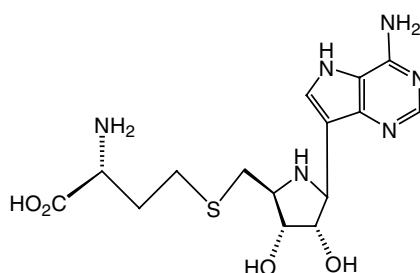


We report the light-activation of allosteric *cis* and *trans* acting ribozymes via decaging of a small organic molecule ligand. To achieve this effectively, we introduce an optimized N-caging group based on a nitrobenzyl core structure. This approach can potentially be employed toward a light-induced control of gene function.

Synthesis of a potent 5'-methylthioadenosine/S-adenosylhomocysteine (MTAN) inhibitor

pp 2662–2665

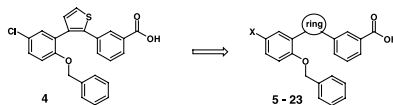
Vivekanand P. Kamath, Jainwen Zhang, Philip E. Morris, Jr. and Y. Sudhakar Babu*



Discovery of novel biaryl heterocyclic EP₁ receptor antagonists

pp 2666–2671

Adrian Hall,* Rino A. Bit, Susan H. Brown, Helene M. Chaignot, Iain P. Chessell, Tanya Coleman, Gerard M.P. Giblin, David N. Hurst, Ian R. Kilford, Xiao Q. Lewell, Anton D. Michel, Shiyam Mohamed, Alan Naylor, Riccardo Novelli, Lee Skinner, David J. Spalding, Sac P. Tang and Richard J. Wilson



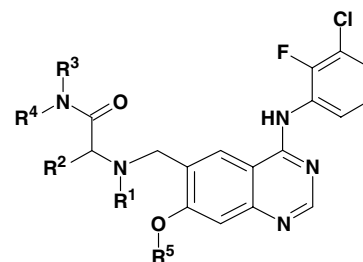
The synthesis and biological activity of a series of novel EP₁ receptor antagonists are described. In vitro and in vivo DMPK data are presented for selected compounds.

Novel 4-anilinoquinazolines with C-6 carbon-linked side chains: Synthesis and structure–activity relationship of a series of potent, orally active, EGF receptor tyrosine kinase inhibitors

pp 2672–2676

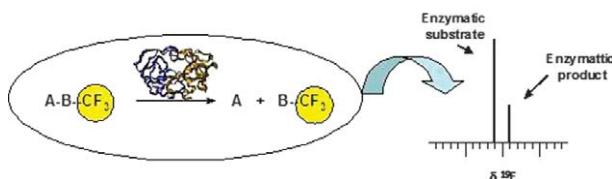
Laurent F. A. Hennequin,* Peter Ballard, F. Tom Boyle, Bénédicte Delouvrié, Rebecca P. A. Ellston, Chris T. Halsall, Craig S. Harris, Kevin Hudson, Jane Kendrew, J. Elizabeth Pease, Helen S. Ross, Peter Smith and Jennifer L. Vincent

The discovery and SAR of a novel subseries of 4-anilinoquinazoline EGFR inhibitors substituted at the C-6 position with carbon-linked side chains are described.

**A fast and robust ¹⁹F NMR-based method for finding new HIV-1 protease inhibitors**

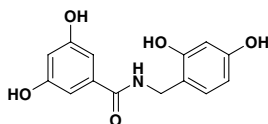
pp 2677–2681

Silvia Frutos, Teresa Tarrago and Ernest Giralt*

**N-Benzylbenzamides: A new class of potent tyrosinase inhibitors**

pp 2682–2684

Sung Jin Cho, Jung Seop Roh, Won Suck Sun, Sung Han Kim and Ki Duk Park*

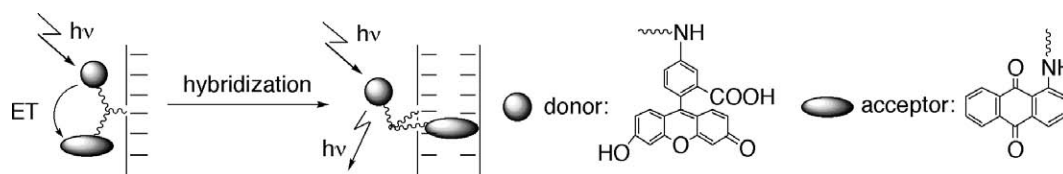


A series of potent inhibitors of tyrosinase and their structure–activity relationships are described. *N*-Benzylbenzamide derivatives (1–21) with hydroxyl(s) were synthesized and tested for their tyrosinase inhibitory activity. With this series, compound **15** provided a potent tyrosinase inhibition: it effectively inhibited the oxidation of L-DOPA catalyzed by mushroom tyrosinase with IC₅₀ of 2.2 μM.

Novel fluorescent oligoDNA probe bearing a multi-conjugated nucleoside with a fluorophore and a non-fluorescent intercalator as a quencher

pp 2685–2688

Sinichi Kodama, Satoko Asano, Tomohisa Moriguchi, Hiroaki Sawai and Kazuo Shinozuka*

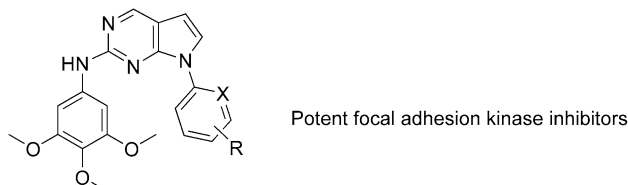


A set of 15mer linear oligoDNA probes bearing a modified nucleoside conjugated with a polyamine/fluorescein/anthraquinone reporting moiety exhibited marked fluorescence signal upon hybridization to the fully complementary stand.

Design and synthesis of 7H-pyrrolo[2,3-d]pyrimidines as focal adhesion kinase inhibitors. Part 2

pp 2689–2692

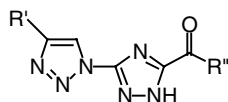
Ha-Soon Choi, Zhicheng Wang, Wendy Richmond, Xiaohui He, Kunyong Yang, Tao Jiang, Donald Karanewsky, Xiang-ju Gu, Vicki Zhou, Yi Liu, Jianwei Che, Christian C. Lee, Jeremy Caldwell, Takanori Kanazawa, Ichiro Umemura, Naoko Matsuura, Osamu Ohmori, Toshiyuki Honda, Nathanael Gray and Yun He*



Discovery of bitriazolyl compounds as novel antiviral candidates for combating the tobacco mosaic virus

pp 2693–2698

Yi Xia, Zhijin Fan, Jianhua Yao, Quan Liao, Wei Li, Fanqi Qu and Ling Peng*



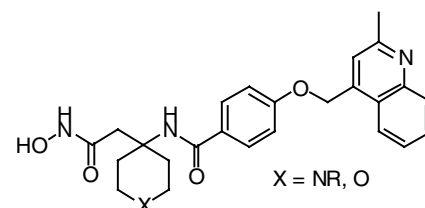
Bitriazolyl compounds have been discovered to show promising antiviral activity against tobacco mosaic virus and may constitute interesting leads for the development of new antiviral candidates.

Synthesis and structure–activity relationship of a novel, achiral series of TNF- α converting enzyme inhibitors

pp 2699–2704

John L. Gilmore,* Bryan W. King, Cathy Harris, Thomas Maduskuie, Stephen E. Mercer, Rui-Qin Liu, Maryanne B. Covington, Mingxin Qian, Maria D. Ribadeneria, Krishna Vaddi, James M. Trzaskos, Robert C. Newton, Carl P. Decicco and James J.-W. Duan

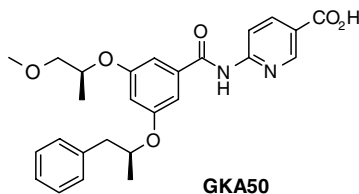
Several series of cyclic- β -aminohydroxamic acids have been synthesized and evaluated for activity against TNF- α -converting enzyme (TACE). The most promising compound exhibits a K_i of 0.35 nM in a pTACE assay and a whole blood activity of 150 nM.



Design of a potent, soluble glucokinase activator with excellent in vivo efficacy

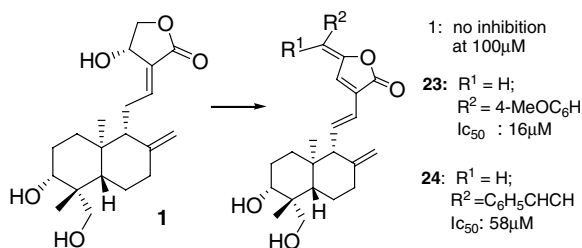
pp 2705–2709

Darren McKerrecher,* Joanne V. Allen, Peter W. R. Caulkett, Craig S. Donald, Mark L. Fenwick, Emma Grange, Keith M. Johnson, Craig Johnstone, Clifford D. Jones, Kurt G. Pike, John W. Rayner and Rolf P. Walker

**Studies on the novel α -glucosidase inhibitory activity and structure–activity relationships for andrographolide analogues**

pp 2710–2713

Gui-Fu Dai, Hai-Wei Xu, Jun-Feng Wang, Feng-Wu Liu and Hong-Min Liu*

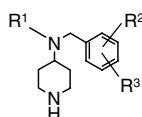


A series of novel α -glucosidase inhibitors were reported and the structure–activity relationships were analyzed.

N-Alkyl-N-arylmethylpiperidin-4-amines: Novel dual inhibitors of serotonin and norepinephrine reuptake

pp 2714–2718

J. R. Boot, S. L. Boulet, B. P. Clark, M. J. Cases-Thomas, L. Delhay, K. Diker, J. Fairhurst, J. Findlay, P. T. Gallagher,* J. Gilmore, J. R. Harris, J. J. Masters, S. N. Mitchell, M. Naik, R. G. Simmonds, S. M. Smith, S. J. Richards, G. H. Timms, M.A. Whatton, C. N. Wolfe and V. A. Wood

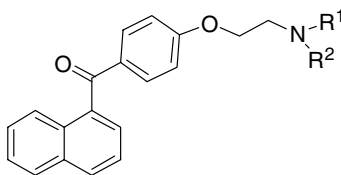


A series of N-alkyl-N-arylmethylpiperidin-4-amines have been prepared and are demonstrated to be inhibitors of both serotonin and norepinephrine reuptake.

Novel substituted naphthalen-1-yl-methanone derivatives as anti-hyperglycemic agents

pp 2719–2723

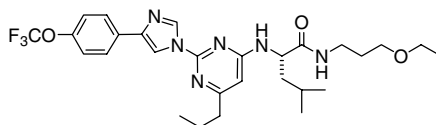
Atul Kumar,* S. R. Pathak, Pervez Ahmad, S. Ray, P. Tewari and A. K. Srivastava



Imidazolylpyrimidine based CXCR2 chemokine receptor antagonists

pp 2724–2728

Koc-Kan Ho,* Douglas S. Auld, Adolph C. Bohnstedt, Paolo Conti, Wim Dokter, Shawn Erickson, Daming Feng, Jim Inglese, Celia Kingsbury, Steven G. Kultgen, Rong-Qiang Liu, Christopher M. Masterson, Michael Ohlmeyer, Yajing Rong, Martijn Rooseboom, Andrew Roughton, Philippe Samama, Martin-Jan Smit, Ellen Son, Jaap van der Louw, Gerard Vogel, Maria Webb, Jac Wijkmans and Ming You



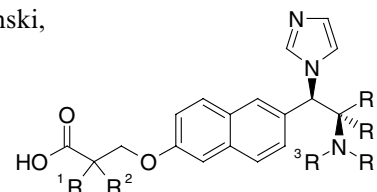
Imidazolylpyrimidine based CXCR2 chemokine receptor antagonist was optimized for potency, in vitro metabolic stability, and oral bioavailability. Potent and orally available CXCR2 antagonists are herein reported.

3-[6-(2-Dimethylamino-1-imidazol-1-yl-butyl)-naphthalen-2-yloxy]-2,2-dimethyl-propionic acid as a highly potent and selective retinoic acid metabolic blocking agent

pp 2729–2733

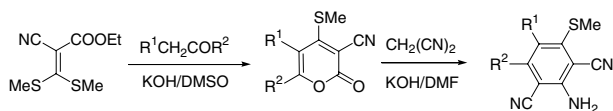
Mark J. Mulvihill,* Julie L. C. Kan, Andrew Cooke, Shripad Bhagwat, Patricia Beck, Mark Bittner, Cara Cesario, David Keane, Viorica Lazarescu, Anthony Nigro, Christy Nillson, Bijoy Panicker, Vanessa Smith, Mary Srebernak, Feng-Lei Sun, Matthew O'Connor, Suzanne Russo, Gia Fischetti, Michael Vrkljan, Shannon Winski, Arlindo L. Castelhana, David Emerson and Neil W. Gibson

3-[6-(2-Dimethylamino-1-imidazol-1-yl-butyl)-naphthalen-2-yloxy]-2,2-dimethyl-propionic acid and analogs were designed and synthesized as highly potent and selective CYP26 inhibitors, serving as retinoic acid metabolic blocking agents (RAMBAs), with demonstrated efficacy in vivo to increase the half-life of exogenous *at*RA.

**Arylanthranilodinitriles: A new biaryl class of antileishmanial agents**

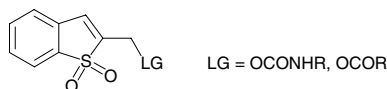
pp 2734–2737

Fateh V. Singh, Rit Vatsyayan, Uma Roy and Atul Goel*

**The Bsmoc group as a novel scaffold for the design of irreversible inhibitors of cysteine proteases**

pp 2738–2741

Jim Iley,* Rui Moreira,* Luísa Martins, Rita C. Guedes and Cláudio M. Soares

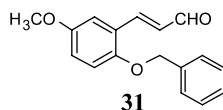


Carbamate and ester derivatives of the 1,1-dioxobenzothiophen-2-ylmethyloxycarbonyl (Bsmoc) scaffold are irreversible inhibitors papain and cathepsin B. In contrast, none of the Bsmoc derivatives inhibited porcine pancreatic elastase, a serine protease.

Synthesis of (2E)-3-{2-[(substituted benzyl)oxy]phenyl}acrylaldehydes as novel anti-inflammatory agents

pp 2742–2747

Li-Jiau Huang,* Jih-Pyang Wang,* Yu-Chi Lai and Sheng-Chu Kuo

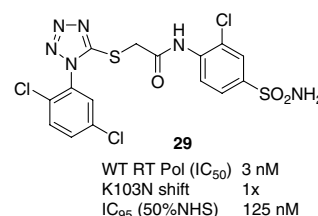


Tetrazole thioacetanilides: Potent non-nucleoside inhibitors of WT HIV reverse transcriptase and its K103N mutant

pp 2748–2752

Ester Muraglia,* Olaf D. Kinzel, Ralph Laufer, Michael D. Miller, Gregory Moyer, Vandna Munshi, Federica Orvieto, Maria Cecilia Palumbi, Giovanna Pescatore, Michael Rowley, Peter D. Williams and Vincenzo Summa

SAR study on tetrazole thioacetanilides as NNRTIs led to potent compounds, with nanomolar activity on both WT HIV and on the clinically relevant K103N mutant, submicromolar activity in infected cells and orally bioavailable in rats.

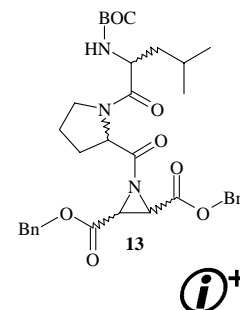


Aziridine-2,3-dicarboxylate inhibitors targeting the major cysteine protease of *Trypanosoma brucei* as lead trypanocidal agents

pp 2753–2757

Radim Vicik, Verena Hoerr, Melanie Glaser, Martina Schultheis, Elizabeth Hansell, James H. McKerrow, Ulrike Holzgrabe, Conor R. Caffrey, Alicia Ponte-Sucre, Heidrun Moll, August Stich and Tanja Schirmeister*

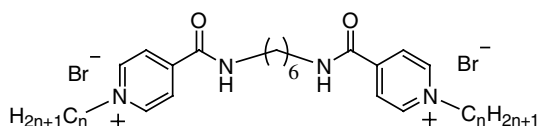
Inhibition of rhodesain, trypanocidal activity, and cytotoxicity against macrophages by cysteine protease inhibitors containing an aziridine-2,3-dicarboxylate moiety are described.



Antimalarial effect of bis-pyridinium salts, N,N'-hexamethylenebis(4-carbamoyl-1-alkylpyridinium bromide)

pp 2758–2760

Kanji Fujimoto, Daiki Morisaki, Munehiro Yoshida, Tetsuto Namba, Kim Hye-Sook, Yusuke Wataya, Hiroki Kourai, Hiroki Kakuta and Kenji Sasaki*

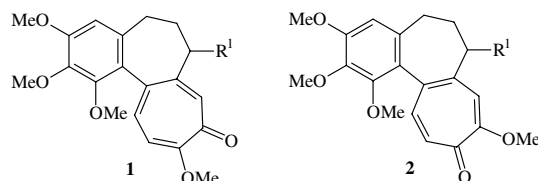


Synthesis and biological evaluation of B-ring modified colchicine and isocolchicine analogs

pp 2761–2764

Michael Cifuentes, Brett Schilling, Rudravajhala Ravindra, Jacquelyn Winter and Mark E. Janik*

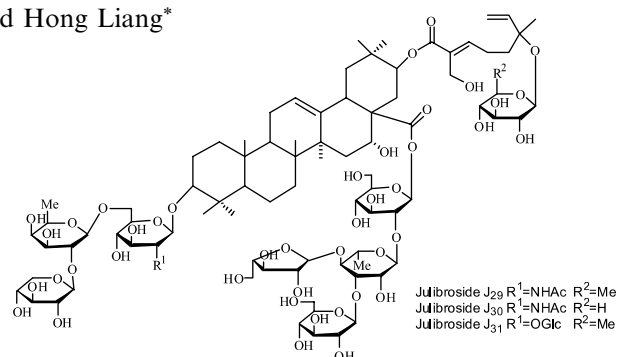
A series of colchicine (**1**) and isocolchicine (**2**) derivatives modified at the B-ring substituent (R^1) were prepared and evaluated in vitro against both microtubule polymerization and PC3 cancer cell lines. The modified colchicine analogs all displayed strong inhibitory activities. More importantly, however, select isocolchicine analogs (**7**, **15**, and **17**) also showed inhibition of microtubule polymerization and **7** exhibited strong cytotoxic activity.

**Three anti-tumor saponins from *Albizia julibrissin***

pp 2765–2768

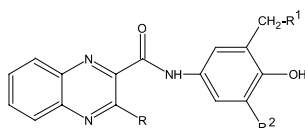
Lu Zheng, Jian Zheng, Yuying Zhao, Bin Wang, Lijun Wu and Hong Liang*

The structures of three new triterpenoid saponins, julibroside J_{29} , julibroside J_{30} , and julibroside J_{31} , isolated from *Albizia julibrissin*, have been determined on the basis of comprehensive spectroscopic analysis. They had marked anti-tumor activity.

**Synthesis and biological evaluation of a novel structural type of serotonin 5-HT₃ receptor antagonists**

pp 2769–2772

Ramachandran Venkatesha Perumal* and Radhakrishnan Mahesh

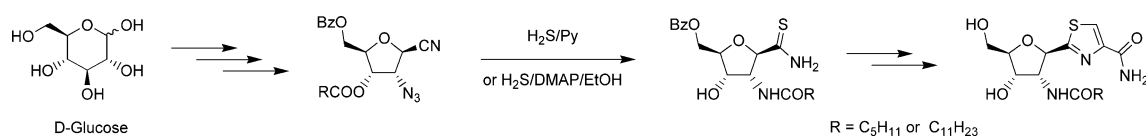


A series of novel 3-substituted quinoxalin-2-carboxamides were prepared and evaluated for serotonin 5-HT₃ receptor antagonist activities in the isolated guinea pig ileum.

Synthesis and antiproliferative activity of two new tiazofurin analogues with 2'-amido functionalities

pp 2773–2776

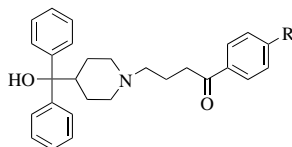
Mirjana Popsavin,* Ljilja Torović, Miloš Svirčev, Vesna Kojić, Gordana Bogdanović and Velimir Popsavin



Design and synthesis of selective, high-affinity inhibitors of human cytochrome P450 2J2

pp 2777–2780

Pierre Lafite, Sylvie Dijols, Didier Buisson, Anne-Christine Macherey,
Darryl C. Zeldin, Patrick M. Dansette and Daniel Mansuy*



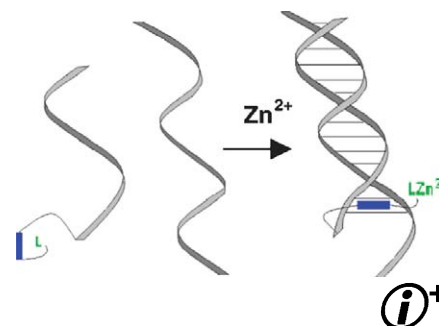
A series of terfenadine analogs were synthesized and evaluated as human CYP2J2 inhibitors. Some of these compounds are high-affinity, selective inhibitors of this enzyme ($R = \text{Pr}$, $K_i = 160 \text{ nM}$).

 Zn^{2+} dependent DNA binders based on terminally modified peptide nucleic acids

pp 2781–2785

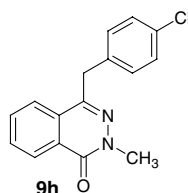
Iris Boll, Larisa Kovbasyuk, Roland Krämer, Thomas Oeser and Andriy Mokhir*

It has been found that affinity of a ligand–intercalator–peptide nucleic acid conjugate to its complementary DNA is affected by Zn^{2+} due to electrostatic interaction between the positively charged $\text{Zn}(\text{ligand})$ complex and the phosphodiester backbone of the DNA.

**Vasorelaxant activity of phthalazinones and related compounds**

pp 2786–2790

Esther del Olmo,* Bianca Barboza, M^a Inés Ybarra, José Luis López-Pérez,
Rosalia Carrón, M^a Angeles Sevilla, Cinthia Boselli and Arturo San Feliciano



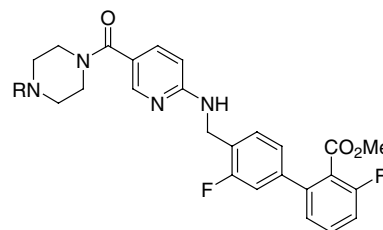
The vasorelaxant activity of some dihydrostilbenamides, imidazo[2,1-*a*]isoindoles, pyrimido[2,1-*a*]isoindoles and phthalazinones has been evaluated. Three phthalazinones reverted the $10 \mu\text{M}$ phenylephrine induced contraction with $\text{EC}_{50} < 1 \mu\text{M}$. The affinities of compound **9h** for α_{1A} , α_{1B} and α_{1D} adrenergic sub-receptors have been determined.

5-Piperazinyl pyridine carboxamide bradykinin B_1 antagonists

pp 2791–2795

Scott D. Kuduk,* Christina Ng Di Marco, Ronald K. Chang, Michael R. Wood, June J. Kim,
Kathy M. Schirripa, Kathy L. Murphy, Richard W. Ransom, Cuyue Tang, Maricel Torrent,
Sookhee Ha, Thomayant Prueksaritanont, Douglas J. Pettibone and Mark G. Bock

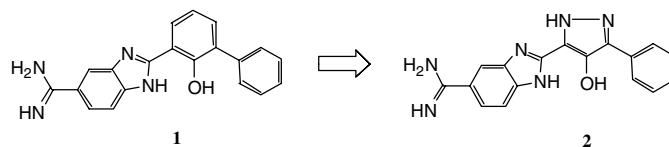
A series of 2,3-diaminopyridine bradykinin B_1 antagonists was modified to mitigate the potential for bioactivation. Removal of the 3-amino group and incorporation of basic 5-piperazinyl carboxamides at the pyridine 5-position provided compounds with high affinity for the human B_1 receptor.



Discovery of novel hydroxy pyrazole based factor IXa inhibitor

pp 2796–2799

Dange Vijaykumar,* Paul A. Sprengeler, Michael Shaghafi, Jeffrey R. Spencer, Brad A. Katz, Christine Yu, Roopa Rai, Wendy B. Young, Brian Schultz and James Janc



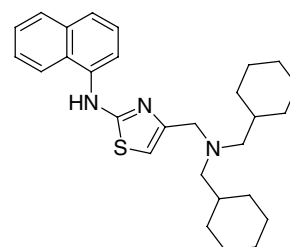
Replacement of central phenol in **1** with hydroxy pyrazole resulted in compound **2** which selectively inhibits factor IXa. It is also selective against trypsin-like serine proteases in the coagulation cascade.

Optimization of 2-aminothiazole derivatives as CCR4 antagonists

pp 2800–2803

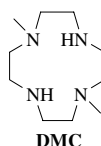
Xuemei Wang, Feng Xu, Qingge Xu, Hossen Mahmud, Jonathan Houze, Liusheng Zhu, Michelle Akerman, George Tonn, Liang Tang, Brian E. McMaster, Daniel J. Dairaghi, Thomas J. Schall, Tassie L. Collins and Julio C. Medina*

A series of 2-aminothiazole-derived antagonists of the CCR4 receptor has been synthesized and their affinity for the receptor evaluated using a [¹²⁵I]TARC (CCL17) displacement assay. Optimization of these compounds for potency and pharmacokinetic properties led to the discovery of potent, orally bioavailable antagonists.

**DNA hydrolysis promoted by 1,7-dimethyl-1,4,7,10-tetraazacyclododecane**

pp 2804–2806

Shu-Hui Wan, Feng Liang,* Xiao-Qin Xiong, Li Yang, Xiao-Jun Wu, Ping Wang, Xiang Zhou* and Cheng-Tai Wu

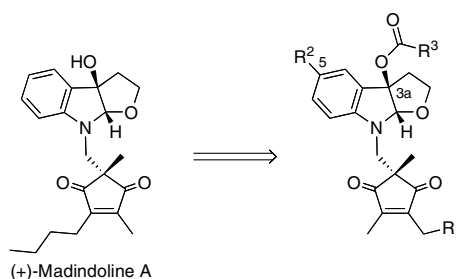


The first metal free macrocyclic polyamine, 1,7-dimethyl-1,4,7,10-tetraazacyclododecane (DMC), was found to hydrolyze DNA under physiological conditions (37 °C, pH 7.2).

Design, synthesis, and biological activities of madindoline analogues

pp 2807–2811

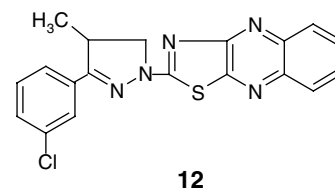
Daisuke Yamamoto, Toshiaki Sunazuka, Tomoyasu Hirose, Naoto Kojima, Eisuke Kaji and Satoshi Omura*



Synthesis, characterization and antiamoebic activity of 1-(thiazolo[4,5-*b*]quinoxaline-2-yl)-3-phenyl-2-pyrazoline derivatives pp 2812–2816

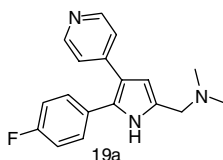
Mohammad Abid and Amir Azam*

New 1-*N*-thiocarboxamide-3-phenyl-2-pyrazolines **1–6** were synthesized by cyclization of different Mannich bases with unsubstituted thiosemicarbazide. The reaction of cyclized pyrazoline derivatives with 2,3-dichloroquinoxaline afforded the title compounds **7–12**. These compounds were subjected to evaluation for their antiamoebic activity. Compound **12** was found to be a better inhibitor of *Entamoeba histolytica* as compared to metronidazole.

**Synthesis and SAR Studies of diarylpyrrole anticoccidial agents**

pp 2817–2821

Xiaoxia Qian,* Gui-Bai Liang, Dennis Feng, Michael Fisher, Tami Crumley, Sandra Rattray, Paula M. Dulski, Anne Gurnett, Penny Sue Leavitt, Paul A. Liberator, Andrew S. Misura, Samantha Samaras, Tamas Tamas, Dennis M. Schmatz, Matthew Wyvratt and Tesfaye Biftu



The dimethylamine-substituted pyrrole **19a** is the most potent inhibitor of *Eimeria tenella* PKG (cGMP-dependent protein kinase) among the diaryl pyrroles evaluated as anticoccidial agents.

OTHER CONTENTS**Erratum**

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Summary of instructions to authors

p I

*Corresponding author

i+ Supplementary data available via ScienceDirect

COVER

View of the crystal structure of the DB819-d(CGCGAATTCGCG)₂ complex, looking down the minor groove of the DNA (see Campbell, N.H.; Evans, D.A.; Lee, M.P.H.; Parkinson, G.N.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2006**, 16, 15.). The DB819 molecule is shown in space-filling mode. Visualisation produced with the VMD program. [Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* **1996**, 14, 33.]

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ISSN 0960-894X