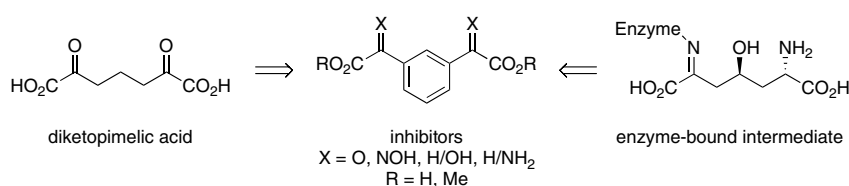


Contents

ARTICLES

Conformationally constrained diketopimelic acid analogues as inhibitors of dihydrodipicolinate synthase pp 460–463

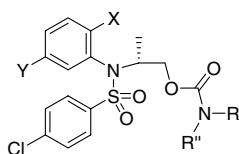
Berin A. Boughton, Renwick C. J. Dobson, Juliet A. Gerrard and Craig A. Hutton*



Carbamate-appended *N*-alkylsulfonamides as inhibitors of γ -secretase

pp 464–468

Carl P. Bergstrom,* Charles P. Sloan, Wai-Yu Lau, David W. Smith, Ming Zheng, Steven B. Hansel, Craig T. Polson, Jason A. Corsa, Donna M. Barten, Kevin M. Felsenstein and Susan B. Roberts

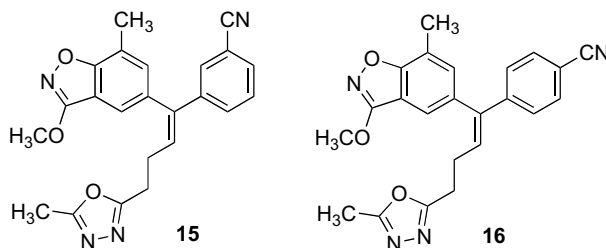


Structure–activity relationships of carbamate-appended *N*-alkylsulfonamide γ -secretase inhibitors are reported.

Inhibition of tubulin polymerization by select alkenyldiarylmethanes

pp 469–473

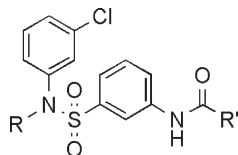
Matthew D. Cullen, Taradas Sarkar, Ernest Hamel, Tracy L. Hartman, Karen M. Watson, Robert W. Buckheit, Jr., Christophe Pannecouque, Erik De Clercq and Mark Cushman*



Design and SAR of selective T-type calcium channel antagonists containing a biaryl sulfonamide core

pp 474–478

Jon J. Hangeland,* Daniel L. Cheney, Todd J. Friends, Stephen Swartz, Paul C. Levesque, Adam J. Rich, Lucy Sun, Terry R. Bridal, Leonard P. Adam, Diane E. Normandin, Natesan Murugesan and William R. Ewing

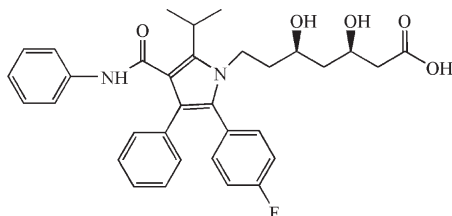


T-type calcium channel antagonists were designed using a protocol involving the program SPROUT constrained by a ComFA-based pharmacophore model. From this exercise, a novel series of potent and selective T-type channel antagonists containing a biaryl sulfonamide core were discovered.

Inhibition of dipeptidyl peptidase-IV (DPP-IV) by atorvastatin

pp 479–484

Tony Taldone, S. William Zito and Tanaji T. Talele*



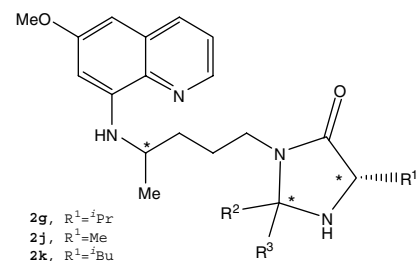
Atorvastatin was determined to be a competitive inhibitor of DPP-IV with $K_i = 57.8 \pm 2.3 \mu\text{M}$.

Anti-*Pneumocystis carinii* and antiparasmodial activities of primaquine-derived imidazolidin-4-ones

pp 485–488

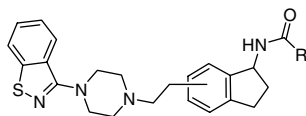
Nuno Vale, Margaret S. Collins, Jiri Gut, Ricardo Ferraz, Philip J. Rosenthal, Melanie T. Cushion, Rui Moreira and Paula Gomes*

The anti-*Pneumocystis carinii* and antiparasmodial activities of compounds **2** were evaluated and found to be correlated. Cycloheptanone-derived imidazolidin-4-ones **2g**, **2j–k** (R^2 and $R^3 = -(\text{CH}_2)_6-$) were the most active.

**1-Aminoindanes as novel motif with potential atypical antipsychotic properties**

pp 489–493

James M. Graham,* Linda L. Coughenour, Bridget M. Barr, David L. Rock and Sham S. Nikam



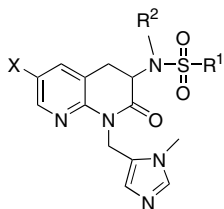
R = alkyls, substituted aryls

As part of an on-going effort to investigate the chemical space requirements for $D_2/5\text{-HT}_{2A}$ receptor antagonists as atypical antipsychotics, new 1-aminoindanes were synthesized. The replacement of the heterocycle (oxindole) in ziprasidone with a carbocycle (indane) was well tolerated and found to retain binding affinities for dopamine D_2 , serotonin 5-HT_{2A} , and serotonin 5-HT_{1A} receptors. Such compounds hold promise as a new chemical motif with atypical antipsychotic properties for the treatment of schizophrenia and related disorders.

2-Oxo-tetrahydro-1,8-naphthyridines as selective inhibitors of malarial protein farnesyltransferase and as anti-malarials

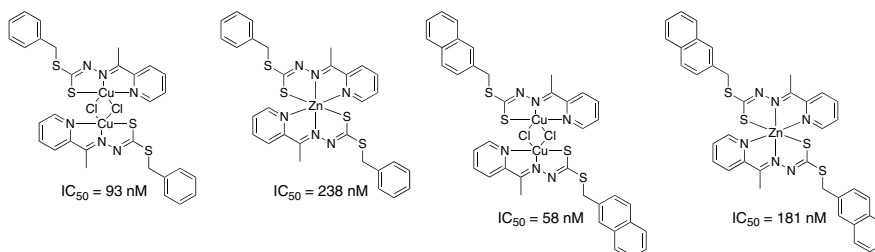
pp 494–497

Srinivas Olepu, Praveen Kumar Suryadevara, Kasey Rivas, Kohei Yokoyama, Christophe L. M. J. Verlinde, Debopam Chakrabarti, Wesley C. Van Voorhis and Michael H. Gelb*

IC₅₀ on malaria protein farnesyltransferase down to 1 nM, ED₅₀ on malaria parasites down to 175 nM.**Synthesis and structure–activity relationships of metal–ligand complexes that potently inhibit cell migration**

pp 498–504

Anwar B. Beshir, Sankar K. Guchhait, José A. Gascón and Gabriel Fenteany*

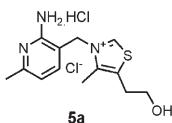


Compounds with antimigratory activity

Prodrug thiamine analogs as inhibitors of the enzyme transketolase

pp 505–508

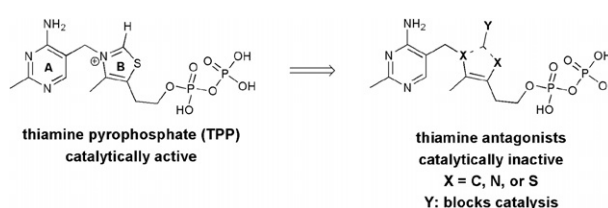
Yvan Le Huerou,* Indrani Gunawardana, Allen A. Thomas, Steven A. Boyd, Jason de Meese, Walter deWolf, Steven S. Gonzales, May Han, Laura Hayter, Tomas Kaplan, Christine Lemieux, Patrice Lee, Jed Pheneger, Gregory Poch, Todd T. Romoff, Francis Sullivan, Solly Weiler, S. Kirk Wright and Jie Lin

Synthesis of prodrugs of the transketolase inhibitor **5a** and their evaluation in murine pharmacokinetic and pharmacodynamic models.**Non-charged thiamine analogs as inhibitors of enzyme transketolase**

pp 509–512

Allen A. Thomas,* J. De Meese, Y. Le Huerou, Steven A. Boyd, Todd T. Romoff, Steven S. Gonzales, Indrani Gunawardana, Tomas Kaplan, Francis Sullivan, Kevin Condroski, Joseph P. Lyssikatos, Thomas D. Aicher, Josh Ballard, Bryan Bernat, Walter DeWolf, May Han, Christine Lemieux, Darin Smith, Solly Weiler, S. Kirk Wright, Guy Vigers and Barb Brandhuber

The synthesis and SAR including structure-based rationale drug design for highly potent non-thiazolium TK antagonists is presented.

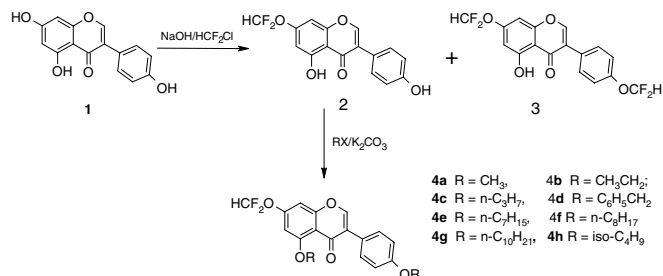


Synthesis of genistein derivatives and determination of their protective effects against vascular endothelial cell damages caused by hydrogen peroxide

pp 513–517

Xiao-Hua Fu, Li Wang, Hong Zhao, Hong-Lin Xiang and Jian-Guo Cao*

A series of novel genistein derivatives were designed and synthesized. Their inhibitory effects were then studied on the hydrogen peroxide induced impairment in human umbilical vein endothelial cells in vitro.

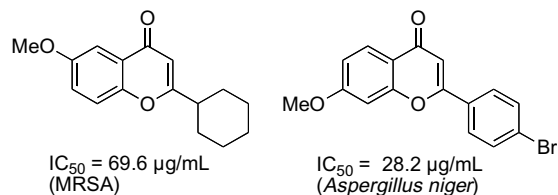


Microwave-assisted synthesis and antimicrobial activities of flavonoid derivatives

pp 518–522

Sherif B. Abdel Ghani, Louise Weaver, Zidan H. Zidan, Hussein M. Ali, C. William Keevil and Richard C. D. Brown*

A series of simple synthetic flavonoid derivatives were found to have significant antifungal activity. Two of the compounds also displayed antibacterial activity against methicillin-resistant *Staphylococcus aureus*.

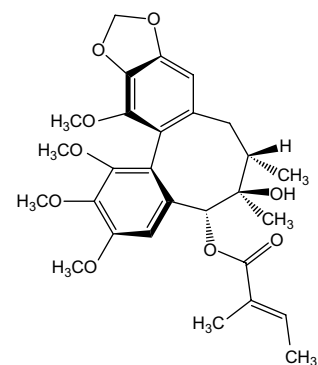


Antiproliferative effects of dibenzocyclooctadiene lignans isolated from *Schisandra chinensis* in human cancer cells

pp 523–526

Hye-Young Min, Eun-Jung Park, Ji-Young Hong, You-Jin Kang, Sun-Jack Kim, Hwa-Jin Chung, Eun-Rhan Woo, Tran Manh Hung, Ui Jung Youn, Yeong Shik Kim, Sam Sik Kang, KiHwan Bae and Sang Kook Lee*

Dibenzocyclooctadiene lignans isolated from *Schisandra chinensis* showed antiproliferative effects in various human cancer cells. The methoxy groups at C-3, C-4, C-3', and C-4', the hydroxyl group at C-8', and the stereo-configuration of the biphenyl ring and the angeloyl group might have influence on these activities. Additional studies indicate that one of mechanism of action of an active compound schizanthrin C in A549 human lung cancer cells was related to the inhibition of cell cycle progression in G0/G1 phase.

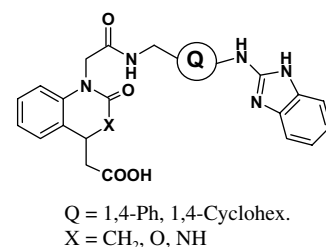


Design and synthesis of novel potent and selective integrin $\alpha_v\beta_3$ antagonists—Novel synthetic routes to isoquinolinone, benzoxazinone, and quinazolinone acetates

pp 527–531

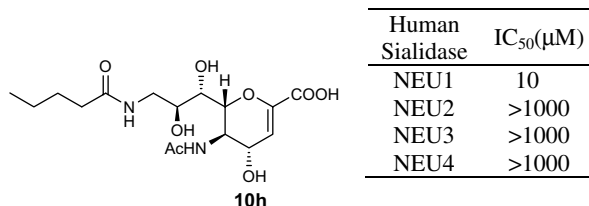
Werner Seitz, Hervé Geneste,* Gisela Backfisch, Jürgen Delzer, Claudia Graef, Wilfried Hornberger, Andreas Kling, Thomas Subkowski and Norbert Zimmermann

An unexpected ring contraction of benzazepinone based $\alpha_v\beta_3$ antagonists led to the design of quinolinone-type derivatives (X = CH₂, O, NH). Novel and efficient synthetic routes to isoquinolinone, benzoxazinone, and quinazolinone acetates were established. Nanomolar $\alpha_v\beta_3$ antagonists based on these new scaffolds were prepared. Moreover, benzoxazinones (X = O) **15a** and **15b** exhibited high microsomal stability and good permeability.



Design, synthesis, and biological evaluation of human sialidase inhibitors. Part 1: Selective inhibitors of lysosomal sialidase (NEU1) pp 532–537

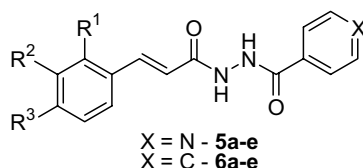
Sadagopan Magesh,* Setsuko Moriya, Tohru Suzuki, Taeko Miyagi, Hideharu Ishida and Makoto Kiso*



The synthesis and human sialidase inhibitory activities of some amide-linked C9 modified DANA analogues **10a–j** are described.

Synthesis and antimycobacterial evaluation of new *trans*-cinnamic acid hydrazide derivatives pp 538–541

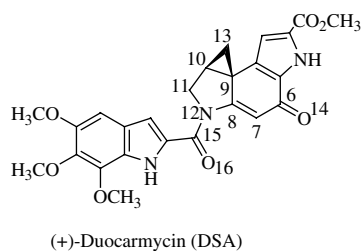
Samir A. Carvalho,* Edson F. da Silva, Marcus V. N. de Souza, Maria C. S. Lourenço and Felipe R. Vicente



The present article describes a series of ten new *trans*-cinnamic acid hydrazide derivatives, which were synthesized and evaluated for their in vitro antibacterial activity against *Mycobacterium tuberculosis*.

Binding free energy calculation for duocarmycin/DNA complex based on the QPLD-derived partial charge model pp 542–545

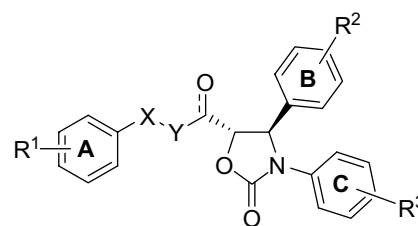
Haizhen Zhong, Karl N. Kirschner, Moses Lee and J. Phillip Bowen*



Substituted oxazolidinones as novel NPC1L1 ligands for the inhibition of cholesterol absorption pp 546–553

Jeffrey A. Pfefferkorn,* Scott D. Larsen, Chad Van Huis, Roderick Sorenson, Tom Barton, Thomas Winters, Bruce Auerbach, Chenyan Wu, Thaddeus J. Wolfram, Hongliang Cai, Kathleen Welch, Nadia Esmail, JoAnn Davis, Richard Bousley, Karl Olsen, Sandra Bak Mueller and Thomas Mertz

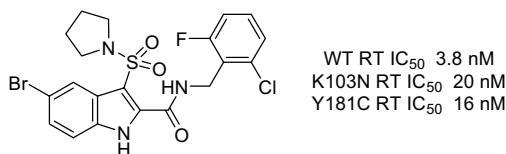
This manuscript describes the synthesis and evaluation of a series of oxazolidinone-based NPC1L1 ligands for the inhibition of cholesterol absorption.



Novel indole-3-sulfonamides as potent HIV non-nucleoside reverse transcriptase inhibitors (NNRTIs)

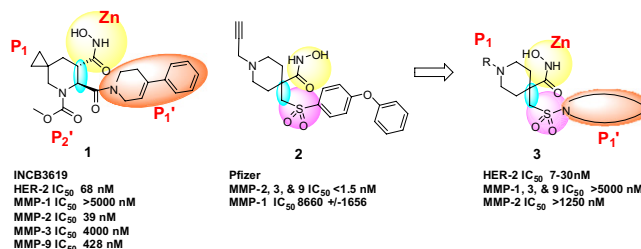
pp 554–559

Zhijian Zhao,* Scott E. Wolkenberg, Meiqing Lu, Vandna Munshi, Gregory Moyer, Meizhen Feng, Anthony V. Carella, Linda T. Ecto, Lori J. Gabryelski, Ming-Tain Lai, Sridar G. Prasad, Youwei Yan, Georgia B. McGaughey, Michael D. Miller, Craig W. Lindsley, George D. Hartman, Joseph P. Vacca and Theresa M. Williams

**Conversion of an MMP-potent scaffold to an MMP-selective HER-2 sheddase inhibitor via scaffold hybridization and subtle P1' permutations**

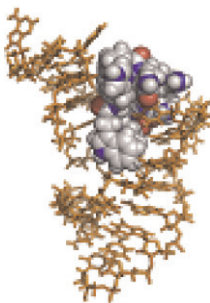
pp 560–564

David M. Burns,* Chunhong He, Yanlong Li, Peggy Scherle, Xiangdong Liu, Cindy A. Marando, Mayanne B. Covington, Gengjie Yang, Max Pan, Sharon Turner, Jordan S. Fridman, Gregory Hollis, Kris Vaddi, Swamy Yeleswaram, Robert Newton, Steve Friedman, Brian Metcalf and Wenqing Yao

**Targeting RNA with cysteine-constrained peptides**

pp 565–567

Virginia A. Burns, Benjamin G. Bobay, Anne Basso, John Cavanagh* and Christian Melander*

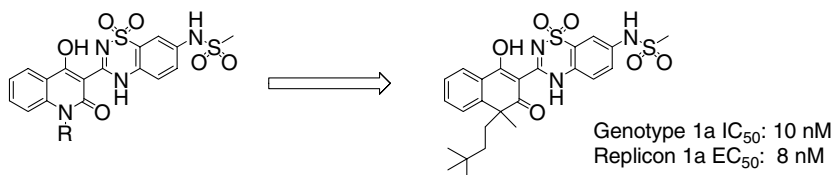


Non poly-cationic cyclic peptides that target RNA are presented.

Synthesis and SAR of novel 1,1-dialkyl-2(1H)-naphthalenones as potent HCV polymerase inhibitors

pp 568–570

Todd D. Bosse,* Daniel P. Larson, Rolf Wagner, Doug K. Hutchinson, Todd W. Rockway, Warren M. Kati, Yaya Liu, Sherie Masse, Tim Middleton, Hongmei Mo, Debra Montgomery, Wen Jiang, Gennadiy Koev, Dale J. Kempf and Akhter Molla



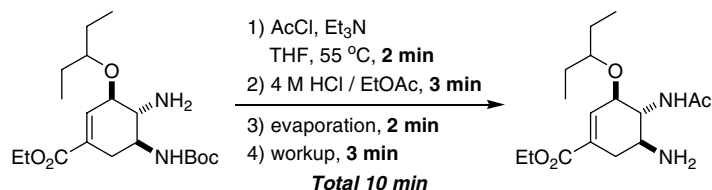
The synthesis and SAR of a series of novel 1,1-dialkyl-2(1H)-naphthalenones as potent HCV polymerase inhibitors is reported.



A method for the synthesis of an oseltamivir PET tracer

pp 600–602

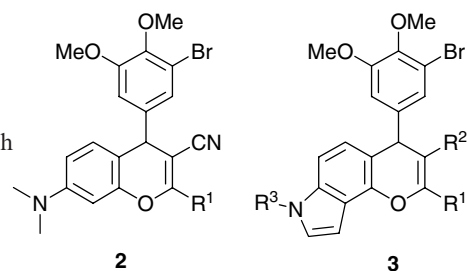
Masataka Morita, Toshihiko Sone, Kenzo Yamatsugu, Yoshihiro Sohtome, Shigeki Matsunaga, Motomu Kanai,* Yasuyoshi Watanabe and Masakatsu Shibasaki

**Discovery of 4-aryl-4*H*-chromenes as a new series of apoptosis inducers using a cell- and caspase-based HTS assay. Part 5: Modifications of the 2- and 3-positions**

pp 603–607

William Kemnitzer, Songchun Jiang, Yan Wang, Shailaja Kasibhatla, Candace Crogan-Grundy, Monica Bubenik, Denis Labrecque, Real Denis, Serge Lamothe, Giorgio Attardo, Henriette Gourdeau, Ben Tseng, John Drewe and Sui Xiong Cai*

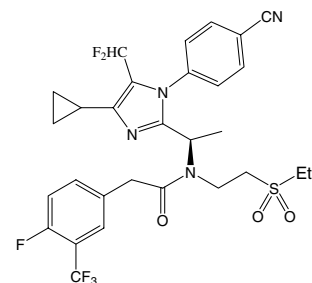
The synthesis and SAR of a group of apoptosis inducing 4-aryl-4*H*-chromenes with modifications at the 2- and 3-positions are reported.

**Design and optimization of imidazole derivatives as potent CXCR3 antagonists**

pp 608–613

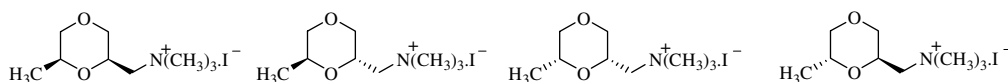
Xiaohui Du, Xiaoqi Chen, Jeffrey T. Mihalic, Jeffrey Deignan, Jason Duquette, An-Rong Li, Bryan Lemon, Ji Ma, Shichang Miao, Karen Ebsworth, Timothy J. Sullivan, George Tonn, Tassie L. Collins and Julio C. Medina*

A series of imidazole derivatives have been designed and optimized for CXCR3 antagonism, pharmacokinetic properties, and reduced formation of glutathione conjugates.

**Rapid novel divergent synthesis and muscarinic agonist profile of all four optical isomers of *N,N,N*-trimethyl(6-methyl-1,4-dioxan-2-yl)methanaminium iodide**

pp 614–618

Alessandro Piergentili,* Wilma Quaglia, Mario Giannella, Fabio Del Bello, Michela Buccioni, Marta Nesi and Rosanna Matucci

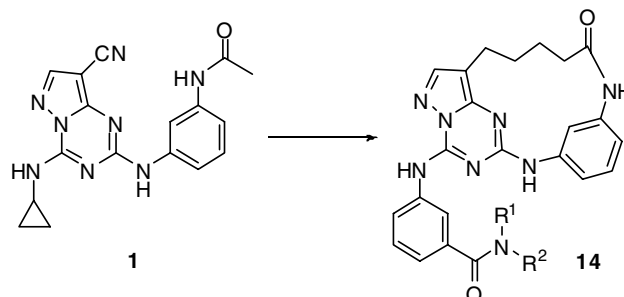


Structure-based design and synthesis of novel macrocyclic pyrazolo[1,5-*a*] [1,3,5]triazine compounds as potent inhibitors of protein kinase CK2 and their anticancer activities

pp 619–623

Zhe Nie, Carin Perretta, Philip Erickson, Stephen Margosiak, Jia Lu, April Averill, Robert Almassy and Shaosong Chu*

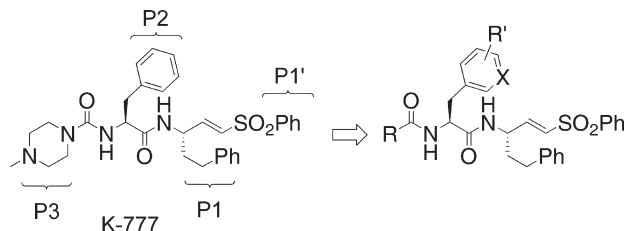
A series of macrocyclic derivatives has been designed and synthesized based on the X-ray co-crystal structures of pyrazolo[1,5-*a*] [1,3,5]triazines with corn CK2 (cCK2) protein. Bioassays demonstrated that these macrocyclic pyrazolo[1,5-*a*] [1,3,5]triazine compounds are potent CK2 inhibitors with K_i around 1.0 nM and they strongly inhibit cancer cell growth with IC_{50} as low as ~100 nM.

**Potency and selectivity of P2/P3-modified inhibitors of cysteine proteases from trypanosomes**

pp 624–628

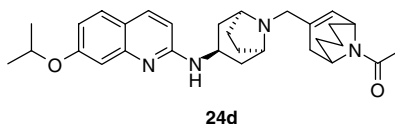
Priyadarshini Jaishankar, Elizabeth Hansell, Dong-Mei Zhao, Patricia S. Doyle, James H. McKerrow and Adam R. Renslo*

A systematic study of P2 and P3 substitution in a series of vinyl sulfone cysteine protease inhibitors is described. The introduction of a methyl substituent in the P2 phenylalanine aryl ring had a favorable effect on protease inhibition and conferred modest selectivity for rhodesain over cruzain. Rhodesain selectivity could be enhanced further by combining these P2 modifications with certain P3 amide substituents.

**Development of CXCR3 antagonists. Part 4: Discovery of 2-amino-(4-tropinyl)quinolines**

pp 629–633

Roland L. Knight,* Daniel R. Allen, Helen L. Birch, Gayle A. Chapman, Frances C. Galvin, Louise A. Jopling, Christopher J. Lock, Johannes W. G. Meissner, David A. Owen, Gilles Raphy, Robert J. Watson and Sophie C. Williams

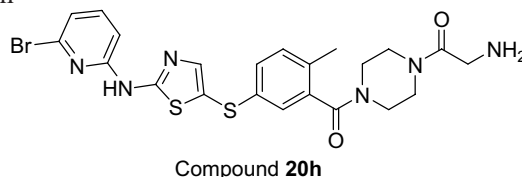


The synthesis and biological evaluation of a novel series of 2-aminoquinoline substituted piperidines and tropanes incorporating a homotropane moiety is herein described. The series exhibits potent antagonism of the CXCR3 receptor and superior physicochemical properties. Compound **24d** was found to be orally bioavailable, and PK/PD studies suggested it as a suitable tool for studying the role of CXCR3 in models of disease.

Identification of 2-amino-5-(thioaryl)thiazoles as inhibitors of nerve growth factor receptor TrkA

pp 634–639

Soong-Hoon Kim,* John S. Tokarski, Kenneth J. Leavitt, Brian E. Fink, Mark E. Salvati, Robert Moquin, Mary T. Obermeier, George L. Trainor, Gregory G. Vite, Linda K. Stadnick, Jonathan S. Lippy, Dan You, Matthew V. Lorenzi and Ping Chen

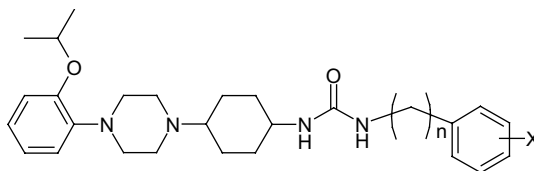


2-Amino-5-(thioaryl)thiazoles are potent inhibitors of TrkA (e.g., **20h**, TrkA IC_{50} = 0.6 nM) that show anti-proliferative effect in cellular assays. A proposed inhibitor binding mode to TrkA active site is consistent with key SAR observations.

(Phenylpiperazinyl)cyclohexylureas: Discovery of $\alpha_{1a/1d}$ -selective adrenergic receptor antagonists for the treatment of benign prostatic hyperplasia/lower urinary tract symptoms (BPH/LUTS)

pp 640–644

George Chiu,* Shengjian Li, Peter J. Connolly, Virginia Pulito, Jingchun Liu and Steven A. Middleton

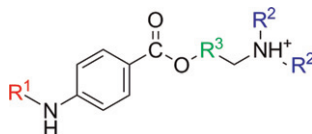


A series of (phenylpiperazinyl)cyclohexylureas that show selectivity to human $\alpha_{1a/1d}$ adrenergic receptors were developed. These compounds have potential for the treatment of BPH/LUTS.

**Block of cyclic nucleotide-gated channels by tetracaine derivatives: Role of apolar interactions at two distinct locations**

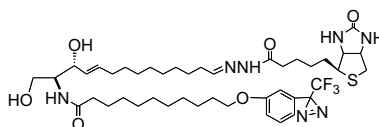
pp 645–649

Timothy Strassmaier, Sarah R. Kirk, Tapasree Banerji and Jeffrey W. Karpen*

**A novel biotinylated diazirinyl ceramide analogue for photoaffinity labeling**

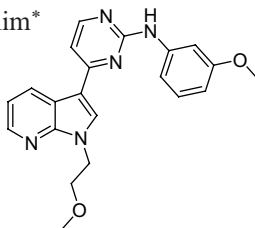
pp 650–652

Makoto Hashimoto* and Yasumaru Hatanaka

**Novel heterocycle-substituted pyrimidines as inhibitors of NF- κ B transcription regulation related to TNF- α cytokine release**

pp 653–656

Hyung-Ho Ha, Jee Seon Kim and B. Moon Kim*

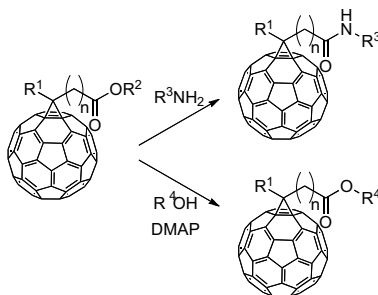
**22**, NF- κ B, IC₅₀ = 1.4 μ M

Novel heterocyclic ring-substituted pyrimidines have been designed as inhibitors of glycogen synthase kinase-3 β and compound **22** exhibited good GSK-3 β and NF- κ B inhibition as well as desirable cellular activity.

Preparation of C₆₀-based active esters and coupling of C₆₀ moiety to amines or alcohols

pp 657–660

Hiroki Tsumoto, Katsumasa Takahashi, Takayoshi Suzuki, Hidehiko Nakagawa, Kohfuku Kohda and Naoki Miyata*



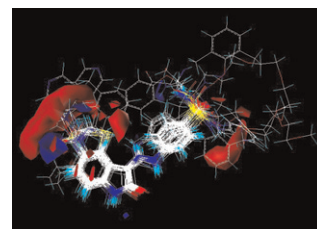
We report the synthesis of C₆₀-based active esters and the coupling of their C₆₀ moiety to various amines or alcohols.

A flavonoid gossypin binds to cyclin-dependent kinase 2

pp 661–664

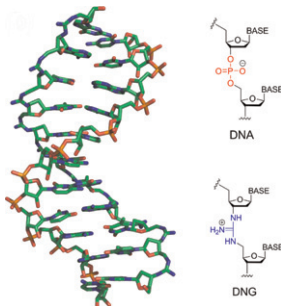
Hojung Kim, Eunjung Lee, Jihye Kim, Bora Jung, Youhoon Chong, Joong-Hoon Ahn and Yoongho Lim*

In order to find flavonoids showing cyclin-dependent kinase 2 (CDK2) binding effects, 347 flavonoid derivatives were docked into the crystal structure of the CDK2. The docking study showed that gossypin has a good conformational match with CDK2, which was confirmed by the binding affinity assay using NMR experiments. In order to find flavonoids showing cyclin-dependent kinase 2 (CDK2) binding effects, 347 flavonoid derivatives were docked into the crystal structure of the CDK2. The docking study showed that gossypin has a good conformational match with CDK2, which was confirmed by the binding affinity assay using NMR experiments.

**Complexation of single strand telomere and telomerase RNA template polyanions by deoxyribonucleic guanidine (DNG) polycations: Plausible anticancer agents**

pp 665–669

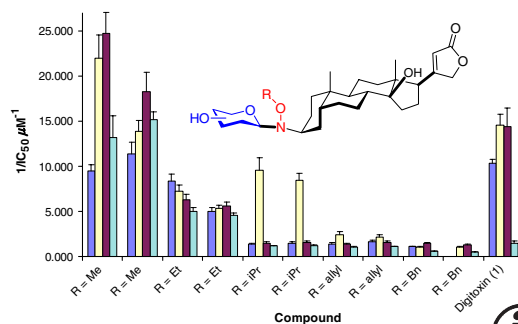
Xiaohua Zhang and Thomas C. Bruice*

**Modifying the glycosidic linkage in digitoxin analogs provides selective cytotoxins**

pp 670–673

Joseph M. Langenhan,* Jeffery M. Engle, Lauren K. Slevin, Lindsay R. Fay, Ryan W. Lucker, Kyle R. Smith and Matthew M. Endo

For the first time a panel of linkage-diversified neoglycosides was constructed. This panel of digitoxin analogs included potent and selective tumor cytotoxins; cytotoxicity was dependent on the structure of the glycosidic linkage.

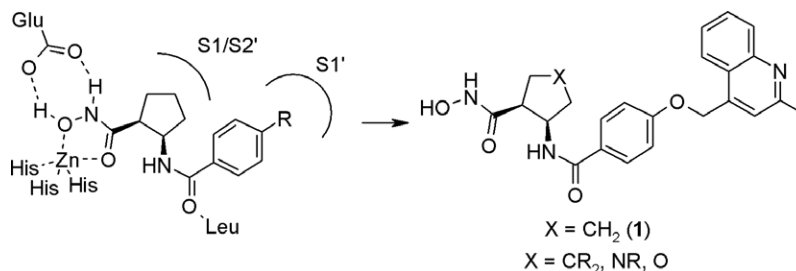


α,β -Cyclic- β -benzamido hydroxamic acids: Novel templates for the design, synthesis, and evaluation of selective inhibitors of TNF- α converting enzyme (TACE)

pp 694–699

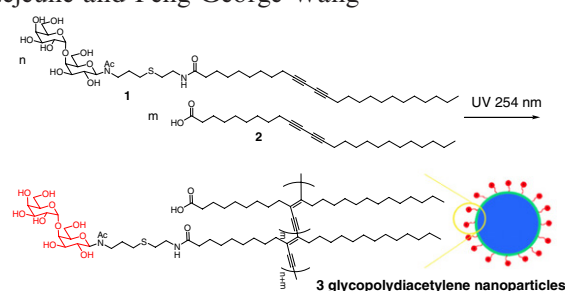
Gregory R. Ott,* Naoyuki Asakawa, Zhonghui Lu, Rui-Qin Liu, Maryanne B. Covington, Krishna Vaddi, Mingxin Qian, Robert C. Newton, David D. Christ, James M. Traskos, Carl P. Decicco and James J.-W. Duan

Selective inhibitors of TNF- α Converting Enzyme (TACE) based on novel α,β -cyclic- β -benzamido hydroxamic acids have been synthesized and evaluated.

**Glycopolydiacetylene nanoparticles as a chromatic biosensor to detect Shiga-like toxin producing *Escherichia coli* O157:H7**

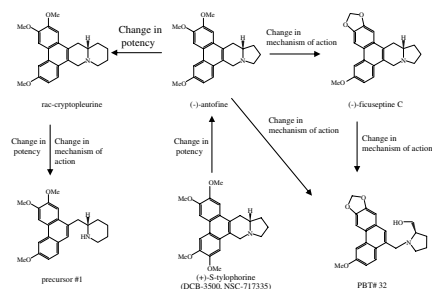
pp 700–703

Jon O. Nagy,* Yalong Zhang, Wen Yi, Xianwei Liu, Edwin Motari, Jing Catherine Song, Jeffrey T. Lejeune and Peng George Wang*

**Structural analogs of tylophora alkaloids may not be functional analogs**

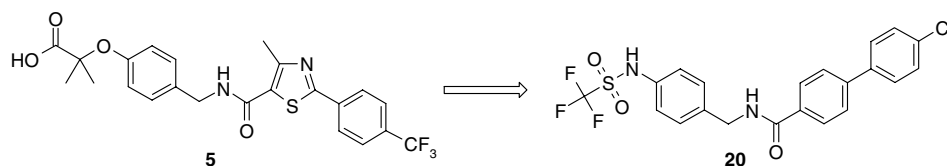
pp 704–709

Wenli Gao, Annie Pei-Chun Chen, Chung-Hang Leung, Elizabeth A. Gullen, Alois Fürstner, Qian Shi, Linyi Wei, Kuo-Hsiung Lee and Yung-Chi Cheng*

**Design, synthesis and evaluation of trifluoromethane sulfonamide derivatives as new potent and selective peroxisome proliferator-activated receptor α agonists**

pp 710–715

Nicolas Faucher,* Paul Martres, Alain Laroze, Olivier Pineau, Florent Potvain and Didier Grillot



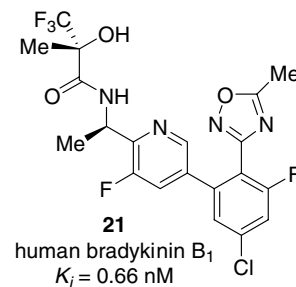
Starting from the structure of **5**, a two-step strategy was applied to identify a new generation of trifluoromethane sulfonamides as potent PPAR α agonists. Synthesis, in vitro and in vivo evaluation of the most potent compound **20** are reported.



α -Hydroxy amides as a novel class of bradykinin B₁ selective antagonists

pp 716–720

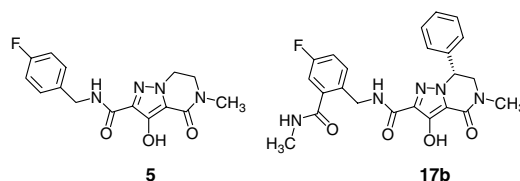
Michael R. Wood,* Kathy M. Schirripa, June J. Kim, Scott D. Kuduk, Ronald K. Chang, Christina N. Di Marco, Robert M. DiPardo, Bang-Lin Wan, Kathy L. Murphy, Richard W. Ransom, Raymond S. L. Chang, Marie A. Holahan, Jacquelynn J. Cook, Wei Lemaire, Scott D. Mosser, Rodney A. Bednar, Cuyue Tang, Thomayant Prueksaritanont, Audrey A. Wallace, Qin Mei, Jian Yu, Dennis L. Bohn, Frank C. Clayton, Emily D. Adarain, Gary R. Sitko, Yvonne M. Leonard, Roger M. Freidinger, Douglas J. Pettibone and Mark G. Bock

**Design and synthesis of substituted 4-oxo-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-2-carboxamides, novel HIV-1 integrase inhibitors**

pp 721–725

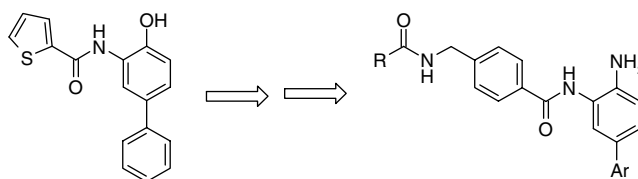
H. Marie Langford,* Peter D. Williams, Carl F. Homnick, Joseph P. Vacca, Peter J. Felock, Kara A. Stillmock, Marc V. Witmer, Daria J. Hazuda, Lori J. Gabryelski and William A. Schleif

A series of 4-oxo-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrazine-2-carboxamides was synthesized and tested for their inhibition of HIV-1 integrase catalytic activity and HIV-1 replication in cells. Structure–activity studies around lead compound **5** indicated that a coplanar relationship of metal-binding heteroatoms provides optimal binding to the integrase active site. Identification of potency-enhancing substituents and adjustments in lipophilicity provided **17b** which inhibits integrase-catalyzed strand transfer with an IC₅₀ value of 74 nM and inhibits HIV-1 replication in cell culture in the presence of 50% normal human serum with an IC₉₅ value of 63 nM.

**Optimization of biaryl Selective HDAC1&2 Inhibitors (SHI-1:2)**

pp 726–731

David J. Witter,* Paul Harrington, Kevin J. Wilson, Melissa Chenard, Judith C. Fleming, Brian Haines, Astrid M. Kral, J. Paul Secrist and Thomas A. Miller

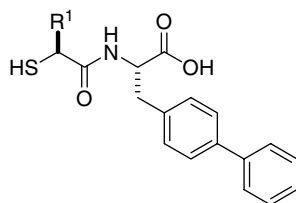


A class of biaryl benzamides was identified and optimized as selective HDAC1&2 inhibitors (SHI-1:2). SAR development based on an initial lead led to a series of potent and selective inhibitors with reduced off-target activity and tumor growth inhibition activity in a HCT-116 xenograft model.

Thiol-based angiotensin-converting enzyme 2 inhibitors: P¹ modifications for the exploration of the S¹ subsite

pp 732–737

David N. Deaton,* Enoch N. Gao, Kevin P. Graham, Jeffrey W. Gross, Aaron B. Miller and John M. Strelow



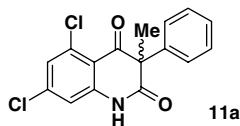
Screening of a metalloprotease library led to the identification of a thiol-based dual ACE/NEP inhibitor as a potent ACE2 inhibitor. Modifications of the P¹ benzyl moiety led to improvements in ACE2 potency as well as to increased selectivity versus ACE and NEP.



Discovery of 3-aryl-3-methyl-1H-quinoline-2,4-diones as a new class of selective 5-HT₆ receptor antagonists

pp 738–743

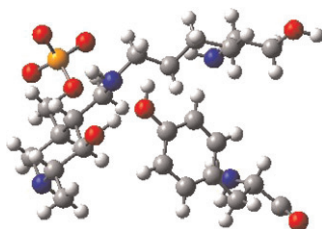
Churl Min Seong,* Woo Kyu Park, Chul Min Park, Jae Yang Kong and No Sang Park



A series of 3-methyl-3-phenyl-1H-quinoline-2,4-diones was prepared and evaluated for 5-HT₆ receptor antagonistic activity.

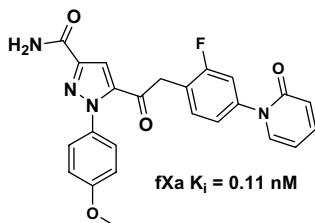
**The first steps. The attack on the carbonyl carbon of pyridoxal cofactor in pyridoxal-dependent enzymes** pp 744–748

Philip E. Sonnet, Linda M. Mascavage and David R. Dalton*

**Structure–activity relationship and pharmacokinetic profile of 5-ketopyrazole factor Xa inhibitors**

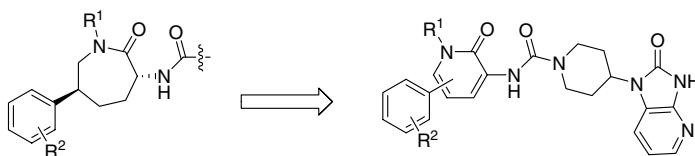
pp 749–754

Jeffrey G. Varnes, Dean A. Wacker,* Donald J. P. Pinto, Michael J. Orwat, Jay P. Therooff, Brian Wells, Robert A. Galemo, Joseph M. Luetgen, Robert M. Knabb, Steven Bai, Kan He, Patrick Y. S. Lam and Ruth R. Wexler

**Calcitonin gene-related peptide (CGRP) receptor antagonists: Investigations of a pyridinone template**

pp 755–758

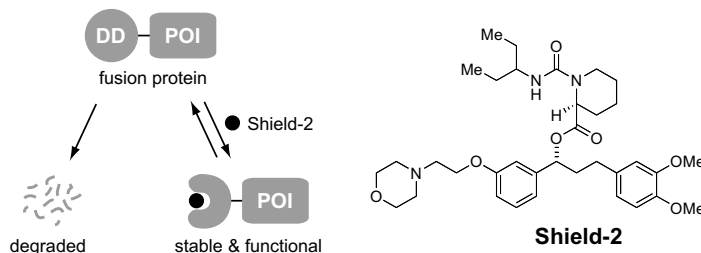
Diem N. Nguyen,* Daniel V. Paone, Anthony W. Shaw, Christopher S. Burgey, Scott D. Mosser, Victor Johnston, Christopher A. Salvatore, Yvonne M. Leonard, Cynthia M. Miller-Stein, Stefanie A. Kane, Kenneth S. Koblan, Joseph P. Vacca, Samuel L. Graham and Theresa M. Williams



Synthesis and analysis of stabilizing ligands for FKBP-derived destabilizing domains

pp 759–761

Joshua S. Grimley, Denise A. Chen, Laura A. Banaszynski and Thomas J. Wandless*

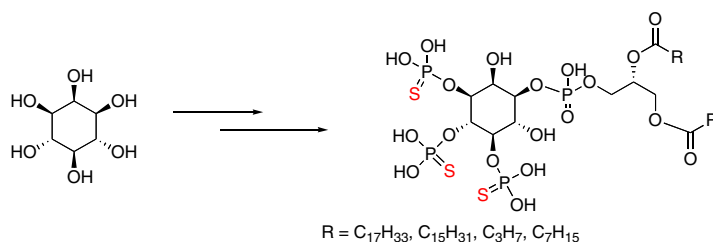


We recently engineered mutants of the FKBP12 protein that are rapidly degraded when expressed in cells. Shield-2 binds to destabilizing domains (DDs) and provides dose-dependent control of their expression levels.

**Synthesis and biological activity of phosphatidylinositol-3,4,5-trisphosphorothioate**

pp 762–766

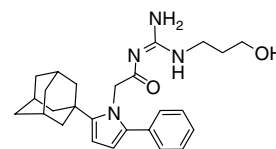
Honglu Zhang, Yong Xu, Nicolas Markadieu, Renaud Beauwens, Christophe Erneux and Glenn D. Prestwich*

**Acylguanidine inhibitors of β -secretase: Optimization of the pyrrole ring substituents extending into the S1' substrate binding pocket**

pp 767–771

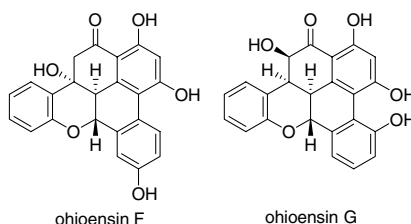
Lee D. Jennings,* Derek C. Cole, Joseph R. Stock, Mohani N. Sukhdeo, John W. Ellingboe, Rebecca Cowling, Guixian Jin, Eric S. Manas, Kristi Y. Fan, Michael S. Malamas, Boyd L. Harrison, Steve Jacobsen, Rajiv Chopra, Peter A. Lohse, William J. Moore, Mary-Margaret O'Donnell, Yun Hu, Albert J. Robichaud, M. James Turner, Erik Wagner and Jonathan Bard

A novel series of acyl guanidines with substituents extending into the S1' substrate binding pocket result in small molecule BACE-1 inhibitors with submicromolar potency and moderate to high selectivity for BACE-1 over cathepsin D.

**Ohioensins F and G: Protein tyrosine phosphatase 1B inhibitory benzonaphthoxanthrenones from the Antarctic moss *Polytrichastrum alpinum***

pp 772–775

Changon Seo, Yun-Hyeok Choi, Jae Hak Sohn, Jong Seog Ahn, Joung Han Yim, Hong Kum Lee and Hyuncheol Oh*

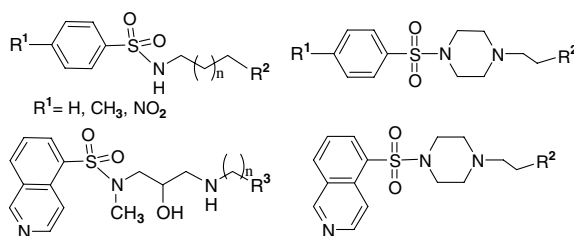


Ohioensins F and G were isolated from *Polytrichastrum alpinum* and evaluated for their PTP1B inhibitory activities.

Design, synthesis and antimalarial activity of benzene and isoquinoline sulfonamide derivatives

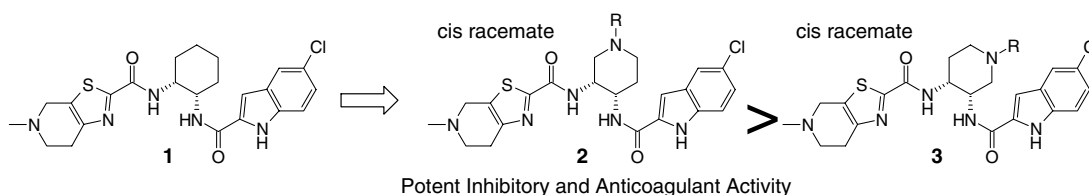
pp 776–781

Maloy Kumar Parai, Gautam Panda,* Kumkum Srivastava and Sunil Kumar Puri

**Design, synthesis, and biological activity of piperidine diamine derivatives as factor Xa inhibitor**

pp 782–787

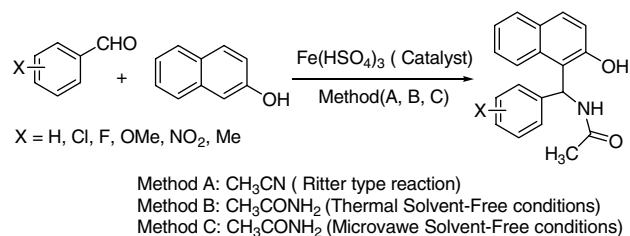
Akiyoshi Mochizuki,* Yumi Nakamoto, Hiroyuki Naito, Kouichi Uoto and Toshiharu Ohta

**An efficient, simple and expedition synthesis of 1-amidoalkyl-2-naphthols as 'drug like' molecules for biological screening**

pp 788–792

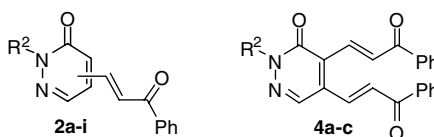
Hamid Reza Shaterian,* Hossein Yarahmadi and Majid Ghashang

An efficient and direct protocol for the preparation of amidoalkyl naphthols employing a multi-component, one-pot condensation reaction of β -naphthol, aromatic aldehydes and acetamide in the presence of ferric hydrogensulfate under solvent, solvent-free and microwave conditions is described. The thermal solvent-free and microwave green procedures offer advantages such as shorter reaction times, simple work-up, excellent yield and recovery and reusability of catalyst. It is noteworthy that 1-amidomethyl-2-naphthols can be converted into important biological 'drug like' active 1-aminomethyl-2-naphthol derivatives by amide hydrolysis.

**2-Substituted 4-, 5-, and 6-[(1E)-3-oxo-3-phenylprop-1-en-1-yl]pyridazin-3(2H)-ones and 2-substituted 4,5-bis[(1E)-3-oxo-3-phenylprop-1-en-1-yl]pyridazin-3(2H)-ones as potent platelet aggregation inhibitors: Design, synthesis, and SAR studies**

pp 793–797

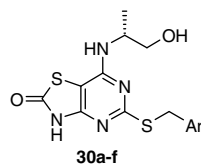
Caroline Meyers, Matilde Yáñez, Abdelaziz Elmaatoui, Tom Verhelst, Alberto Coelho, Nuria Fraiz, Guy L. F. Lemièrre, Xerardo García-Mera, Reyes Laguna, Ernesto Cano, Bert U. W. Maes and Eddy Sotelo*



Evaluation of a series of bicyclic CXCR2 antagonists

pp 798–803

Iain Walters,* Caroline Austin, Rupert Austin, Roger Bonnert, Peter Cage, Mark Christie, Mark Ebdon, Stuart Gardiner, Caroline Grahames, Steven Hill, Fraser Hunt, Robert Jewell, Shirley Lewis, Iain Martin, David Nicholls and David Robinson

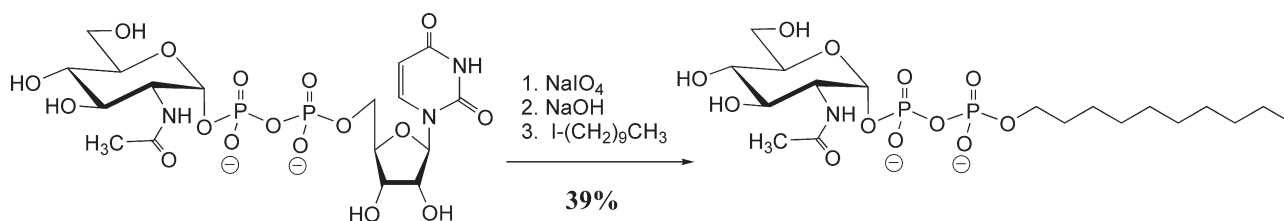


The SAR of a series of pyrimidine-based fused bicyclic heterocycles at the CXCR2 receptor was investigated, leading to the discovery of a series of potent, bioavailable thiazolo[4,5-*d*]pyrimidine-2(3*H*)-one antagonists **30a-f** with additional CCR2 activity.

A very simple synthesis of GlcNAc- α -pyrophosphoryl-decanol: A substrate for the assay of a bacterial galactosyltransferase

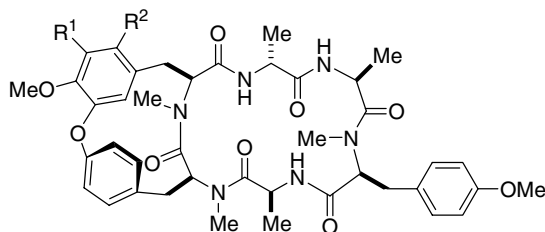
pp 804–807

Inka Brockhausen, E. Andreas Larsson and Ole Hindsgaul*

**A novel bicyclic hexapeptide, RA-XVIII, from *Rubia cordifolia*: Structure, semi-synthesis, and cytotoxicity**

pp 808–811

Ji-Ean Lee, Yukio Hitotsuyanagi, Ik-Hwi Kim, Tomoyo Hasuda and Koichi Takeya*



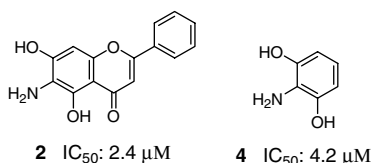
RA-XVIII: R¹ = OH, R² = H

analogues: R¹, R² = H, OH, NH₂, NO₂

2-Aminoresorcinol is a potent α -glucosidase inhibitor

pp 812–815

Hong Gao and Jun Kawabata*

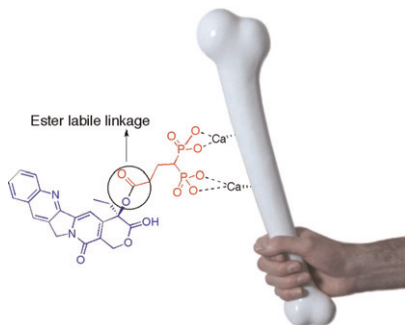


The 2-aminoresorcinol moiety of 6-amino-5,7-dihydroxyflavone (**2**) is important to exert the α -glucosidase inhibitory activity and 2-aminoresorcinol (**4**), itself, is a potent α -glucosidase inhibitor.

Chemotherapeutic bone-targeted bisphosphonate prodrugs with hydrolytic mode of activation

pp 816–820

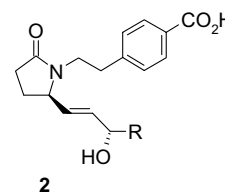
Rotem Erez, Sharon Ebner, Bernard Attali and Doron Shabat*

**Synthesis and evaluation of a γ -lactam as a highly selective EP₂ and EP₄ receptor agonist**

pp 821–824

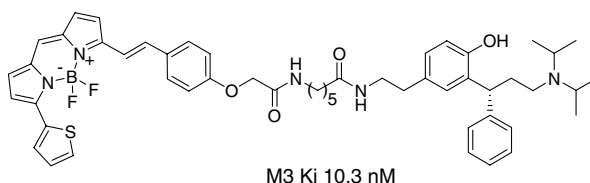
Yufang Xiao,* Gian Luca Araldi, Zhong Zhao, Adulla Reddy, Srinivasa Karra, Nadia Brugger, David Fischer, Elizabeth Palmer, Bagna Bao and Sean D. McKenna

γ -Lactam analogs (**2**) of EP₄ receptor agonists were identified by substitution of the pyrazolidinone ring (**1**) with a pyrrolidinone ring. Several compounds (such as **2a**, **2h**) with high potency, selectivity, and acceptable PK profiles were discovered. These were assessed in animal models of ovulation induction and bronchoconstriction.

**Design and synthesis of a fluorescent muscarinic antagonist**

pp 825–827

Lyn H. Jones,* Amy Randall, Carolyn Napier, Mike Trevethick, Sasha Sreckovic and Jessica Watson



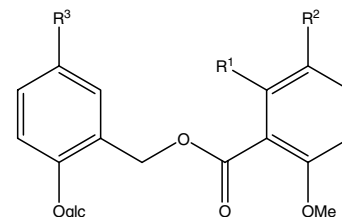
The design and concise synthesis of a potent and fluorescent BODIPY-tolterodine conjugate antimuscarinic probe is reported.

New polyphenols active on β -amyloid aggregation

pp 828–831

Céline Rivière, Tristan Richard, Xavier Vitrac, Jean-Michel Mérillon, Josep Valls and Jean-Pierre Monti*

Four novel polyphenols could be efficient fibril inhibitors in Alzheimer's disease: malvidin and its glucoside and curculigosides B and D. Moreover, molecules with the particular C₆-linkers-C₆ structure could be potent inhibitors.



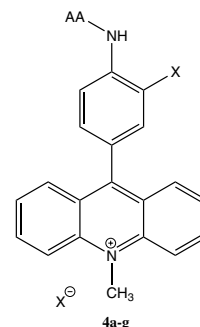
	R ¹	R ²	R ³	
12	OMe	H	OH	curculigoside A
13	OH	H	OH	curculigoside B
14	OMe	OH	H	curculigoside D

Synthesis and evaluation of novel chromogenic peptidase substrates based on 9-(4'-aminophenyl)-10-methylacridinium salts as diagnostic tools in clinical bacteriology

pp 832–835

Rosaleen J. Anderson,* Paul W. Groundwater, Yongxue Huang, Arthur L. James, Sylvain Orenge, Annette Rigby, Céline Roger-Dalbert and John D. Perry

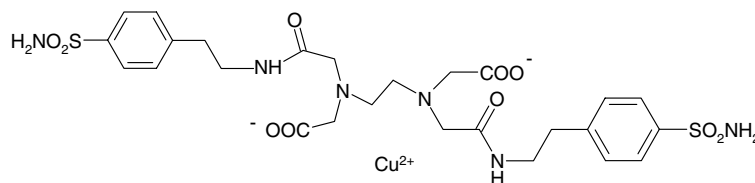
The synthesis and evaluation of novel chromogenic peptidase substrates **4a–g** with good species specificity are described.



Carbonic anhydrase inhibitors: Copper(II) complexes of polyamino-polycarboxylamido aromatic/heterocyclic sulfonamides are very potent inhibitors of the tumor-associated isoforms IX and XII

pp 836–841

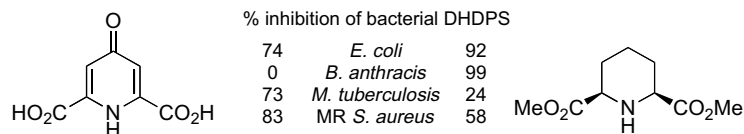
Marouan Rami, Jean-Yves Winum,* Alessio Innocenti, Jean-Louis Montero, Andrea Scozzafava and Claudiu T. Supuran*



Inhibiting dihydrodipicolinate synthase across species: Towards specificity for pathogens?

pp 842–844

Voula Mitsakos, Renwick C. J. Dobson, F. Grant Pearce, Sean R. Devenish, Genevieve L. Evans, Benjamin R. Burgess, Matthew A. Perugini, Juliet A. Gerrard and Craig A. Hutton*

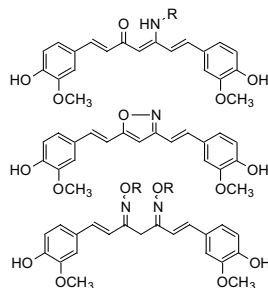


Inhibitors of dihydrodipicolinate synthase (DHDPS), a key enzyme in lysine biosynthesis and an important antibiotic target, display significant species-specificity.

Antitumor effects of curcumin and structurally β -diketone modified analogs on multidrug resistant cancer cells

pp 845–849

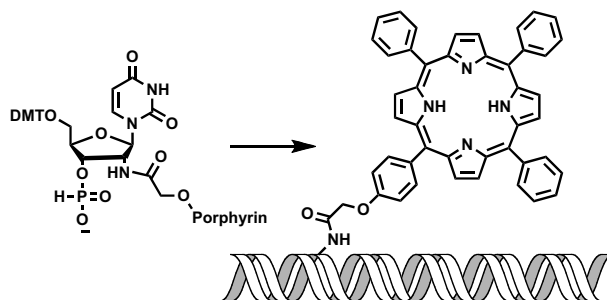
Daniele Simoni,* Michele Rizzi, Riccardo Rondanin, Riccardo Baruchello, Paolo Marchetti, Francesco Paolo Invidiata, Manuela Labbozzetta, Paola Poma, Valeria Carina, Monica Notarbartolo, Alessandra Alaimo and Natale D'Alessandro



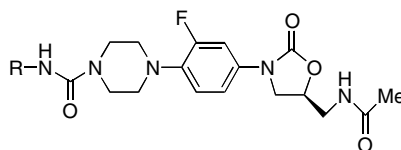
Porphyrin conjugated to DNA by a 2'-amido-2'-deoxyuridine linkage

pp 850–855

Sarita Sitaula and Scott M. Reed*

**Synthesis, SAR, and antibacterial activity of novel oxazolidinone analogues possessing urea functionality** pp 856–860

N. Selvakumar,* G. Govinda Rajulu, K. Chandra Shekar Reddy, B. Chandra Chary, P. Kalyan Kumar, T. Madhavi, K. Praveena, K. Hari Prasada Reddy, Mohammed Takhi, Arundhuti Mallick, P. V. S. Amarnath, Sreenivas Kandepu and Javed Iqbal



The syntheses of a series of novel oxazolidinone analogues possessing an urea functionality are reported. The SAR around the urea functional group resulted in interesting antibacterial compounds.

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

p I

*Corresponding author

Supplementary data available via ScienceDirect

COVER

Overlay of high resolution co-crystal structures of *R*-**22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, 17, 5677.]

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