Bioorganic & Medicinal Chemistry Letters

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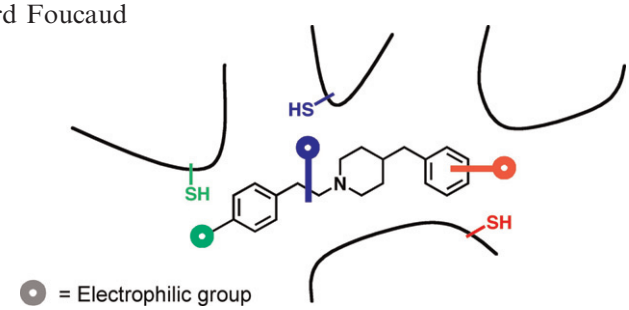
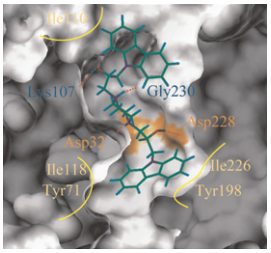
Reactive derivatives for affinity labeling in the ifenprodil site of NMDA receptors pp 2765–2770
Karine Alarcon,* Adeline Martz, Laetitia Mony, Jacques Neyton, Pierre Paoletti, Maurice Goeldner and Bernard Foucaud

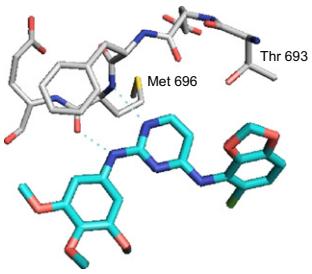


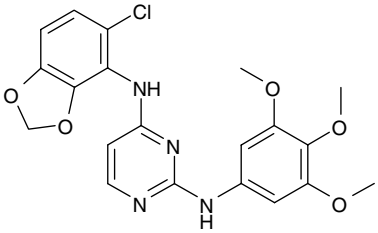
In silico multi-filter screening approaches for developing novel β-secretase inhibitors pp 2771–2775
Taku Fujimoto, Yasuo Matsushita, Hiroaki Gouda, Noriyuki Yamaotsu and Shuichi Hirono*

A large database of chemical structures was screened for potential novel inhibitors of β-secretase using in silico multi-filter techniques. Compounds with a calculated strong binding free energy to β-secretase were selected as 'hits'. The hits included all the compounds already identified as β-secretase inhibitors in the database, which validates the effectiveness of our in silico screening methods.



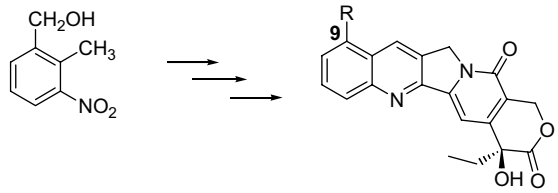
Inhibitors of the tyrosine kinase EphB4. Part 1: Structure-based design and optimization of a series of 2,4-*bis*-anilinopyrimidines pp 2776–2780
Catherine Bardelle, Darren Cross, Sara Davenport, Jason G. Kettle,* Eun Jung Ko, Andrew G. Leach, Andrew Mortlock, Jon Read, Nicola J. Roberts, Peter Robins and Emma J. Williams





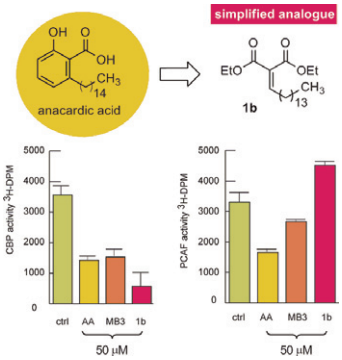
7: EphB4 IC_{50} = 0.24 μM

Synthesis and cytotoxic activity of new 9-substituted camptothecins pp 2781–2787
Sabrina Dallavalle,* Daniela Granza Rocchetta, Loana Musso, Lucio Merlini, Gabriella Morini, Sergio Penco, Stella Tinelli, Giovanni Luca Beretta and Franco Zunino



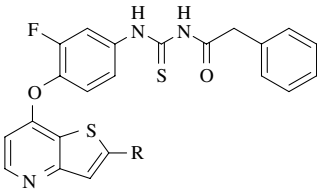
Identification of long chain alkylidenemalonates as novel small molecule modulators of histone acetyltransferases pp 2788–2792
Gianluca Sbardella,* Sabrina Castellano, Caterina Vicidomini, Dante Rotili, Angela Nebbioso, Marco Miceli, Lucia Altucci* and Antonello Mai*

Pentadecylidenemalonate **1b** is the first histone acetyltransferases (HAT) modulator able to potentiate PCAF (GNAT family) activity while inhibiting that of CBP (p300/CBP family).

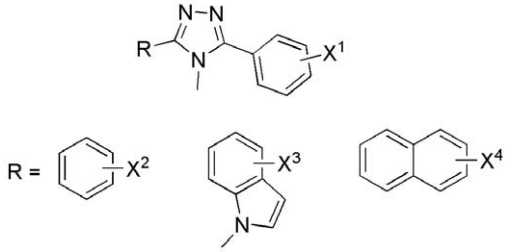


Discovery of a novel and potent series of thieno[3,2-*b*]pyridine-based inhibitors of c-Met and VEGFR2 tyrosine kinases pp 2793–2798
Stephen Claridge,* Franck Raeppel, Marie-Claude Granger, Naomy Bernstein, Oscar Saavedra, Lijie Zhan, David Llewellyn, Amal Wahhab, Robert Deziel, Jubrail Rahil, Normand Beaulieu, Hannah Nguyen, Isabelle Dupont, Annie Barsalou, Carole Beaulieu, Ian Chute, Serge Gravel, Marie-France Robert, Sylvain Lefebvre, Marja Dubay, Roussen Pascal, Jeff Gillespie, Zhiyun Jin, James Wang, Jeffrey M. Besterman, A. Robert MacLeod and Arkadii Vaisburg

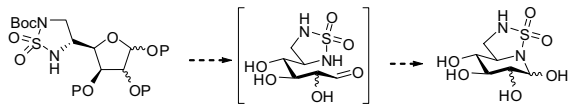
The synthesis and biological evaluation of a series of thieno[3,2-*b*]pyridine inhibitors of the tyrosine kinases c-Met and VEGRF2 is described.



Bis-aryl triazoles as selective inhibitors of 11β-hydroxysteroid dehydrogenase type 1 pp 2799–2804
Susan D. Aster,* Donald W. Graham, Divya Kharbanda, Gool Patel, Mitree Ponpipom, Gina M. Santorelli, Michael J. Szymonifka, Steven S. Mundt, Kashmira Shah, Marty S. Springer, Rolf Thieringer, Anne Hermanowski-Vosatka, Samuel D. Wright, Jianying Xiao, Hratch Zokian and James M. Balkovec

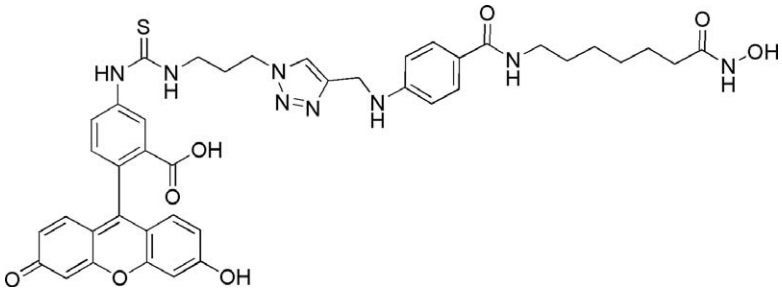


Synthesis and evaluation of sulfamide-type indolizidines as glycosidase inhibitors **pp 2805–2808**
Mahmoud Benltifa, M. Isabel García Moreno, Carmen Ortiz Mellet,* José M. García Fernández and Anne Wadouachi*

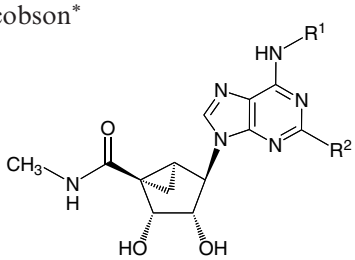


Novel sulfamide-type indolizidine glycomimetics with a selective α-mannosidase inhibition.

Development of a fluorescence polarization based assay for histone deacetylase ligand discovery **pp 2809–2812**
Ralph Mazitschek, Vishal Patel, Dyann F. Wirth and Jon Clardy*

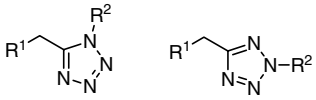


Design of (N)-methanocarba adenosine 5′-uronamides as species-independent A_3 receptor-selective agonists **pp 2813–2819**
Artem Melman, Zhan-Guo Gao, Deepmala Kumar, Tina C. Wan, Elizabeth Gizewski, John A. Auchampach and Kenneth A. Jacobson*



R^1 = Me, MeO, substituted benzyl and 2-phenylethyl, R^2 = Cl, I, MeS, alkynyl.

New tetrazole-based selective anandamide uptake inhibitors **pp 2820–2824**
Giorgio Ortar,* Aniello Schiano Moriello, Maria Grazia Cascio, Luciano De Petrocellis, Alessia Ligresti, Enrico Morera, Marianna Nalli and Vincenzo Di Marzo

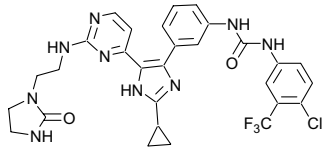


R^1 = 4-biphenyl, biphenyl-4-carboxamido

R^2 = $CH_2CON(CH_3)_2$, CH_2COCH_3, $CH_2CH(CH_3)_2$, CH_2CN, $CH_2CO_2CH_3$

A new series of 1,5-and 2,5-disubstituted tetrazoles have been synthesized and evaluated as inhibitors of anandamide cellular uptake. Some of them inhibit the uptake process with a relatively high potency (IC_{50} = 2.3–5.1 μM) and selectively over other proteins involved in the endocannabinoids activity and metabolism.

Dual binding site inhibitors of B-RAF kinase pp 2825–2829
Ronald L. Wolin,* Scott D. Bembenek, Jianmei Wei, Shelby Crawford, Katherine Lundeen, Anders Brunmark, Lars Karlsson, James P. Edwards and Jonathan M. Blevitt

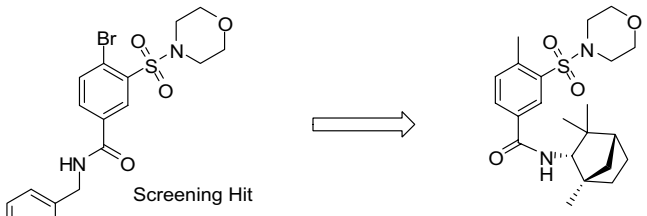


11, K_i (B-RAF) = 66 nM

Diarylimidazole motifs were designed to interact with both the ATP binding site and the adjacent allosteric region.

Sulfamoyl benzamides as novel CB_2 cannabinoid receptor ligands pp 2830–2835
Karin Worm,* Q. Jean Zhou, Christopher T. Saeui, Rosalyn C. Green, Joel A. Cassel, Gabriel J. Stabley, Robert N. DeHaven, Nathalie Conway-James, Christopher J. LaBuda, Michael Koblish, Patrick J. Little and Roland E. Dolle

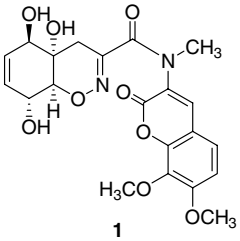
A series of novel sulfamoyl benzamide cannabinoid ligands was synthesized and their biological activity determined.



Screening Hit
K_i CB_1 > 1000 nM
K_i CB_2 = 800 nM

K_i CB_1 = 130 nM, EC_{50} = 550 nM
K_i CB_2 = 3.9 nM, EC_{50} = 4.6 nM

The isolation, structure determination and cytotoxicity of the new fungal metabolite, trichodermamide C pp 2836–2839
Rohan A. Davis,* James Longden, Vicky M. Avery and Peter C. Healy

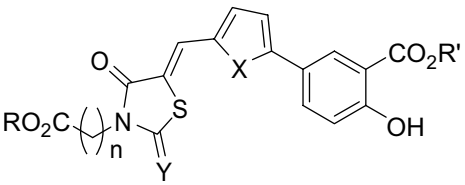


1

The new fungal metabolite, trichodermamide C **1** was shown by high content screening to display cytotoxicity towards the human colorectal carcinoma HCT116 and human lung carcinoma A549 with IC_{50} values of 0.68 and 4.28 μg/ml, respectively.

Discovery of a novel submicromolar inhibitor of the lymphoid specific tyrosine phosphatase pp 2840–2844
Yuli Xie, Yidong Liu, Gangli Gong, Alison Rinderspacher, Shi-Xian Deng, Deborah H. Smith, Udo Toebben, Effie Tzilianos, Lars Branden, Dušica Vidović, Caty Chung, Stephan Schürer, Lutz Tautz and Donald W. Landry*

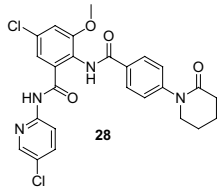
A series of small molecule inhibitors of the lymphoid specific tyrosine phosphatase were described.



8a-8s(IC_{50}=0.39-44uM)
R, R'=H, CH_3
n=0, 1, 2

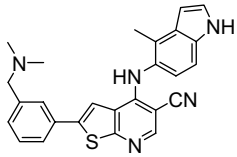
Structure–activity relationships of anthranilamide-based factor Xa inhibitors containing piperidinone and pyridinone P4 moieties pp 2845–2849

James R. Corte,* Tianan Fang, Donald J. P. Pinto, Wei Han, Zilun Hu, Xiang-Jun Jiang, Yun-Long Li, Jolicia F. Gauuan, Mark Hadden, Darren Orton, Alan R. Rendina, Joseph M. Luettgen, Pancras C. Wong, Kan He, Paul E. Morin, Chong-Hwan Chang, Daniel L. Cheney, Robert M. Knabb, Ruth R. Wexler and Patrick Y. S. Lam



Synthesis and PKCθ inhibitory activity of a series of 4-(indol-5-ylamino)thieno[2,3-*b*]pyridine-5-carbonitriles pp 2850–2853

Diane H. Boschelli,* Biqi Wu, Ana Carolina Barrios Sosa, Joan Chen, Magda Asselin, Derek C. Cole, Julie Lee, Xiaoke Yang and Divya Chaudhary

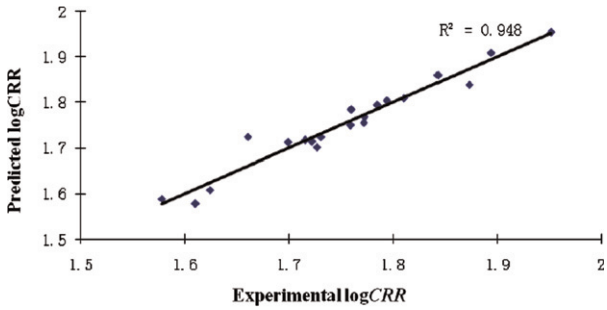


Of a series of 4-(indol-5-ylamino)thieno[2,3-*b*]pyridine-5-carbonitriles, the most potent PKCθ inhibitory activity was observed with compound **29**.

QSAR study of mosquito repellents from terpenoid with a six-member-ring pp 2854–2859

Zongde Wang, Jie Song,* Jinzhu Chen, Zhanqian Song, Shibin Shang, Zhikuan Jiang and Zhaojiu Han

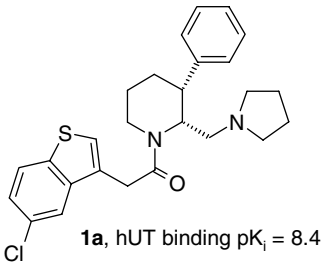
QSAR modeling has been applied to 20 mosquito repellents from α- and β-pinene in turpentine oils. The best qualitative model obtained includes four parameters.



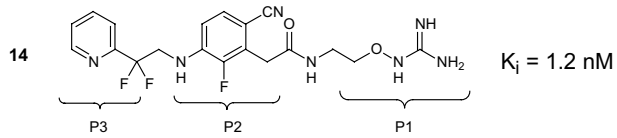
2-Aminomethyl piperidines as novel urotensin-II receptor antagonists pp 2860–2864

Jian Jin,* Yonghui Wang, Feng Wang, Dongchuan Shi, Karl F. Erhard, Zining Wu, Brian F. Guida, Sarah K. Lawrence, David J. Behm, Jyoti Disa, Kalindi S. Vaidya, Christopher Evans, Lynette J. McMillan, Ralph A. Rivero, Michael J. Neeb and Stephen A. Douglas

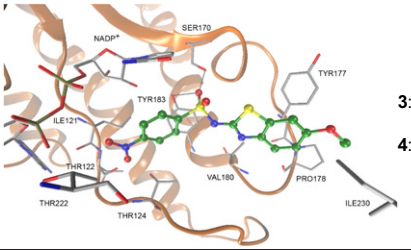
A series of 2-aminomethyl piperidines has been discovered as novel urotensin-II receptor antagonists. The synthesis, initial structure-activity relationships, and optimization of the initial hit that resulted in the identification of potent, cross-species active, and functional urotensin-II receptor antagonists such as **1a** are described.

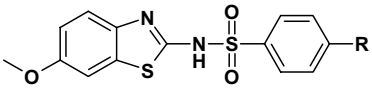


Orally efficacious thrombin inhibitors with cyanofluorophenylacetamide as the P2 motif pp 2865–2870
Kevin D. Kreutter, Tianbao Lu, Lily Lee, Edward C. Giardino, Sharmila Patel, Hui Huang, Guozhang Xu, Mark Fitzgerald, Barbara J. Haertlein, Venkatraman Mohan, Carl Crysler, Stephen Eisennagel, Malini Dasgupta, Martin McMillan, John C. Spurlino, Norman D. Huebert, Bruce E. Maryanoff, Bruce E. Tomczuk, Bruce P. Damiano and Mark R. Player*

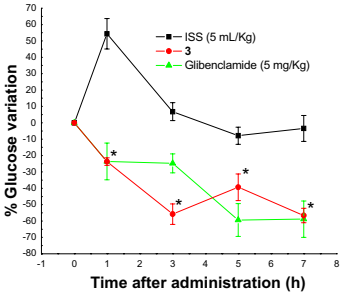


Antidiabetic activity of *N*-(6-substituted-1,3-benzothiazol-2-yl)benzenesulfonamides pp 2871–2877
Hermenegilda Moreno-Díaz, Rafael Villalobos-Molina, Rolffy Ortiz-Andrade, Daniel Díaz-Coutiño, Jose Luis Medina-Franco, Scott P. Webster, Margaret Binnie, Samuel Estrada-Soto, Maximiliano Ibarra-Barajas, Ismael León-Rivera and Gabriel Navarrete-Vázquez*



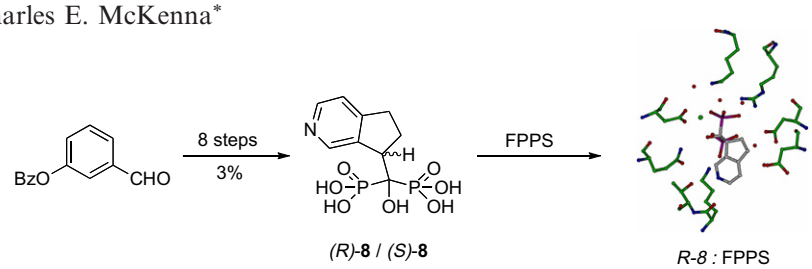


3: R=-H; % of inhibition 11-βHSD1 @ 10μM =37.63
Orally active @ 100mg/Kg
4: R= -NO_2; % of inhibition 11-βHSD1 @ 10μM = 53.32
Orally active @ 100mg/Kg

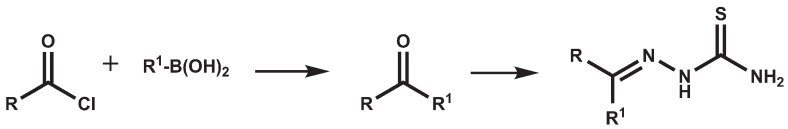


Farnesyl pyrophosphate synthase enantiospecificity with a chiral risedronate analog, [6,7-dihydro-5*H*-cyclopenta[*c*]pyridin-7-yl(hydroxy)methylene]bis(phosphonic acid) (NE-10501): Synthetic, structural, and modeling studies pp 2878–2882
Sylvine Deprèle, Boris A. Kashemirov, James M. Hogan, Frank H. Ebetino, Bobby L. Barnett, Artem Evdokimov and Charles E. McKenna*

Racemic **8**, synthesized by an improved method, is preferentially bound to its inhibitor target, FPPS, as the (*R*) enantiomer (X-ray structure), confirming a stereo-specific interaction predicted by a docking simulation.



Discovery of trypanocidal thiosemicarbazone inhibitors of rhodesain and TbcatB pp 2883–2885
Jeremy P. Mallari, Anang Shelat, Aaron Kosinski, Conor R. Caffrey, Michele Connelly, Fangyi Zhu, James H. McKerrow and R. Kiplin Guy*



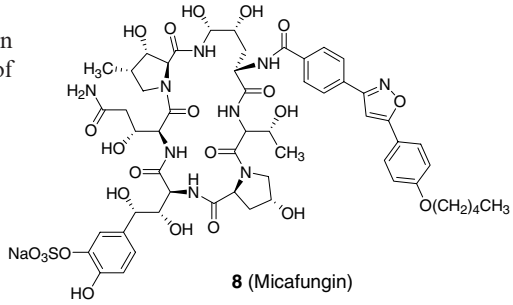
R = 4-Me Ph, R^1 = 3-CF_3 Ph

IC_{50} TbcatB	= 210 nM
IC_{50} rhodesain	= 8 nM
IC_{50} cathepsin L	= 9 nM
IC_{50} cathepsin B	= 210 nM
EC_{50} T.brucei	= 1500 nM
EC_{50} BJ	>25000 nM
EC_{50} Raji	>25000nM
EC_{50} HEK 293	>25000 nM
EC_{50} HEP G2	>25000 nM

Novel echinocandin antifungals. Part 2: Optimization of the side chain of the natural product FR901379. Discovery of micafungin pp 2886–2890

Masaki Tomishima,* Hidenori Ohki, Akira Yamada, Katsuyuki Maki and Fumiaki Ikeda

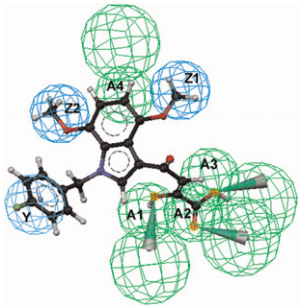
Further optimization of the potent antifungal activity of side chain analogs of the natural product FR901379 led to the discovery of compound **8** (micafungin) with an excellent, well-balanced profile.



A refined pharmacophore model for HIV-1 integrase inhibitors: Optimization of potency in the 1H-benzylindole series pp 2891–2895

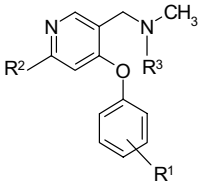
Laura De Luca, Maria Letizia Barreca, Stefania Ferro, Nunzio Iraci, Martine Michiels, Frauke Christ, Zeger Debyser, Myriam Witvrouw and Alba Chimirri*

The development of a new three-dimensional pharmacophore model for HIV-1 integrase inhibitors and the synthesis of some 4-[1-(4-fluorobenzyl)-1*H*-indol-3-yl]-2-hydroxy-4-oxobut-2-enoic acids is reported.



Pyridyl-phenyl ether monoamine reuptake inhibitors: Impact of lipophilicity on dual SNRI pharmacology and off-target promiscuity pp 2896–2899

Gavin A. Whitlock,* Paul V. Fish, M. Jonathan Fray, Alan Stobie and Florian Wakenhut



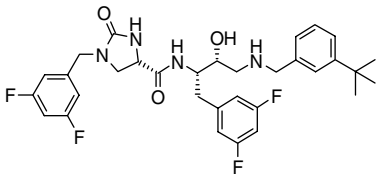
clogP >3.5 for balanced SNRI activity

Promiscuous off-target pharmacology

A novel series of pyridyl-phenyl ethers are disclosed, which possess potent dual 5-HT and NA reuptake pharmacology with good selectivity over dopamine reuptake inhibition. The series was found to possess significant polypharmacology issues, we concluded that this off-target promiscuity was related to high lipophilicity.

Synthesis, SAR, and X-ray structure of human BACE-1 inhibitors with cyclic urea derivatives pp 2900–2904

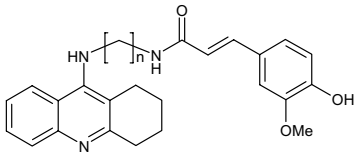
Heuisul Park,* Kyeongsik Min,* Hyo-Shin Kwak, Ki Dong Koo, Dongchul Lim, Sang-Won Seo, Jae-Ung Choi, Bettina Platt and Deog-Young Choi



26

Compound **26** showed excellent inhibitory activity against BACE-1, good selectivity over Cathepsin D.

Design and synthesis of tacrine–ferulic acid hybrids as multi-potent anti-Alzheimer drug candidates pp 2905–2909
Lei Fang, Birgit Kraus, Jochen Lehmann, Joerg Heilmann, Yihua Zhang* and Michael Decker*

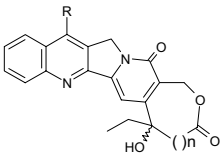


6a, n=2; **6b**, n=3; **6c**, n=4;
6d, n=5; **6e**, n=8

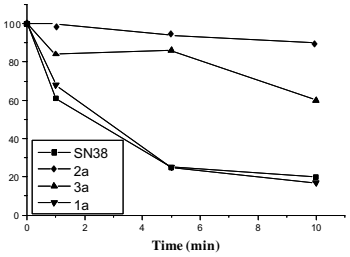
Novel ChE inhibitory (IC_{50}: AChE 4.4–38.6 nM; BChE 5.9–34.1 nM) and antioxidant (0.4–2.0 equiv to Trolox)tacrine–ferulic acid hybrids are reported.

E-ring-modified 7-oxyiminomethyl camptothecins: Synthesis and preliminary in vitro and in vivo biological evaluation pp 2910–2915
Giuseppe Giannini,* Mauro Marzi, Walter Cabri, Elena Marastoni, Gianfranco Battistuzzi, Loredana Vesci, Claudio Pisano, Giovanni Luca Beretta, Michelandrea De Cesare and Franco Zunino*

Using a panel of human tumor cells, 7-oxyiminomethyl derivatives of homocamptothecins showed a potent antiproliferative activity correlating to persistence of the cleavable complex.



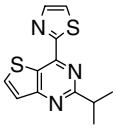
1a. n = 1, R = H
2a. n = 1, R = CH=NOtBu
3a. n = 1, R = CH=NOCH$_2$Ph



Antagonists of the human adenosine A_{2A} receptor. Part 1: Discovery and synthesis of thieno[3,2-*d*]pyrimidine-4-methanone derivatives pp 2916–2919
Roger J. Gillespie, David R. Adams, David Bebbington, Karen Benwell, Ian A. Cliffe, Claire E. Dawson, Colin T. Dourish, Allan Fletcher, Suneel Gaur, Paul R. Giles, Allan M. Jordan,* Antony R. Knight, Lars J. S. Knutsen, Anthony Lawrence, Joanne Lerpiniere, Anil Misra, Richard H. P. Porter, Robert M. Pratt, Robin Shepherd, Rebecca Upton, Simon E. Ward, Scott M. Weiss and Douglas S. Williamson

The (−)-enantiomer of the antimalarial drug mefloquine is a potent and moderately selective antagonist of the adenosine A_{2A} receptor. Further investigation of this compound has revealed a series of potent and selective keto-aryl thieno[3,2-*d*]pyrimidine derivatives which show promising activity in a commonly used model of Parkinson's disease.

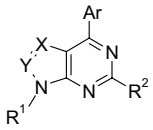
Antagonists of the human adenosine A_{2A} receptor. Part 2: Design and synthesis of 4-arylthieno[3,2-*d*]pyrimidine derivatives pp 2920–2923
Roger J. Gillespie, Ian A. Cliffe, Claire E. Dawson, Colin T. Dourish, Suneel Gaur, Paul R. Giles, Allan M. Jordan,* Antony R. Knight, Anthony Lawrence, Joanne Lerpiniere, Anil Misra, Robert M. Pratt, Richard S. Todd, Rebecca Upton, Scott M. Weiss and Douglas S. Williamson



The design and synthesis of a series of biaryl thieno[3,2-*d*]pyrimidines is described. These novel compounds are potent adenosine A_{2A} receptor antagonists and show high degrees of selectivity against human A_1, A_{2B} and A_3 receptors. Moreover, a number of these compounds show promising activity in in vivo models of Parkinson's disease.

Antagonists of the human adenosine A_{2A} receptor. Part 3: Design and synthesis of pyrazolo[3,4-*d*]pyrimidines, pyrrolo[2,3-*d*]pyrimidines and 6-arylpurines **pp 2924–2929**

Roger J. Gillespie, Ian A. Cliffe, Claire E. Dawson, Colin T. Dourish, Suneel Gaur, Allan M. Jordan, Antony R. Knight, Joanne Lerpiniere, Anil Misra, Robert M. Pratt, Jonathan Roffey, Gemma C. Stratton, Rebecca Upton, Scott M. Weiss and Douglas S. Williamson*

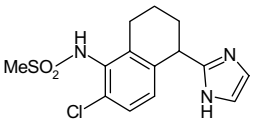


A series of pyrazolo[3,4-*d*]pyrimidine, pyrrolo[2,3-*d*]pyrimidine and 6-arylpurine adenosine A_{2A} antagonists is described. Many examples were highly selective against the human A_1 receptor sub-type and were active in an in vivo model of Parkinson's disease.

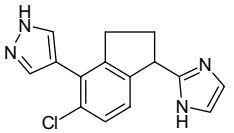
Novel 2-imidazoles as potent and selective α_{1A} adrenoceptor partial agonists **pp 2930–2934**

Gavin A. Whitlock,* Kelly Conlon, Gordon McMurray, Lee R. Roberts, Alan Stobie and Richard J. Thurlow

A series of novel 2-imidazoles is described, which combine potent and selective α_{1A} partial agonist pharmacology with good drug-like properties.



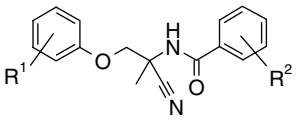
α_{1A} EC_{50} 43nM
α_{1A} Emax 61%
α_{1B} EC_{50} >10000nM
α_{1D} EC_{50} >10000nM
α_{2A} EC_{50} >10000nM



α_{1A} EC_{50} 78nM
α_{1A} Emax 52%
α_{1B} EC_{50} >10000nM
α_{1D} EC_{50} >10000nM
α_{2A} EC_{50} >10000nM

Discovery of amino-acetonitrile derivatives, a new class of synthetic anthelmintic compounds **pp 2935–2938**

Pierre Ducray, Noëlle Gauvry,* François Pautrat, Thomas Goebel, Joerg Fruechtel, Yves Desaules, Sandra Schorderet Weber, Jacques Bouvier, Trixie Wagner, Olivier Froelich and Ronald Kaminsky

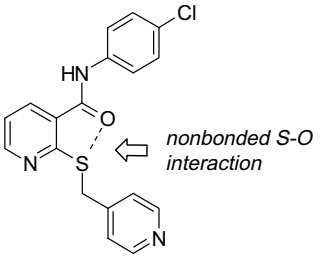


The discovery and SAR of a new series of amino-acetonitrile derivatives (AAD) potent against parasitic nematode species are reported.

Conformation–activity relationship on novel 4-pyridylmethylthio derivatives with antiangiogenic activity **pp 2939–2943**

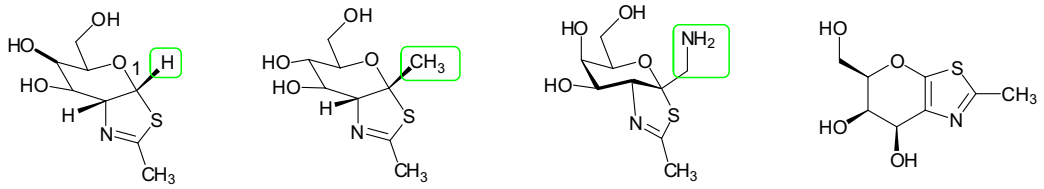
Takahiro Honda,* Hisashi Tajima, Yasushi Kaneko, Masakazu Ban, Takaaki Inaba, Yuriko Takeno, Kazuyoshi Okamoto and Hiroyuki Aono

Conformation–activity relationship on novel 4-pyridylmethylthio derivative **1** with antiangiogenic activity and the related compounds is reported.



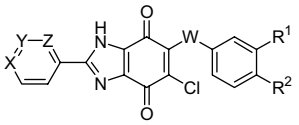
1 (KDR, IC_{50} = 26 nM)

N-Acetylhexosaminidase inhibitory properties of C-1 homologated GlcNAc- and GalNAc-thiazolines pp 2944–2947
Benjamin Amorelli, Chunhua Yang, Brian Rempel, Stephen G. Withers and Spencer Knapp*



Several C-l homologated pyranose-fused thiazolines and a GalNAc-thiazole were evaluated as inhibitors of the bacterial *N*-acetylhexosaminidase SpHex; kinetic analysis suggests active site steric restrictions around the anomeric carbon.

Design, synthesis and evaluation of 2-phenyl-1*H*-benzo[*d*]imidazole-4,7-diones as vascular smooth muscle cell proliferation inhibitors pp 2948–2951
Chung-Kyu Ryu,* Ra-Young Lee, Seung-Yon Lee, Hwa-Jin Chung, Sang Kook Lee and Kwang-Hoe Chung



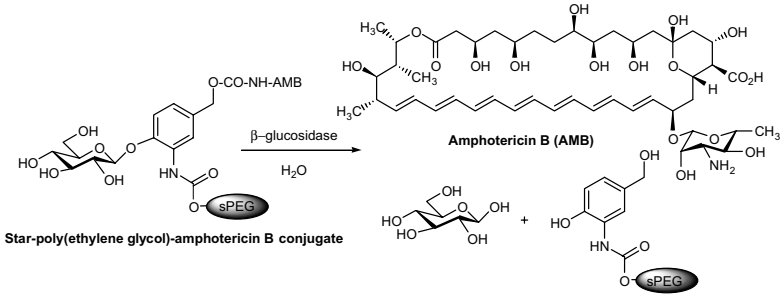
R^1, R^2 = H, F, Cl, ..

X,Y, Z= N or CH; W= NH or S

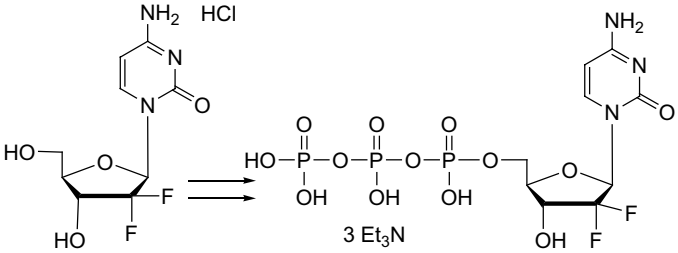
2-Phenyl-1*H*-benzo[*d*]imidazole-4,7-diones were synthesized and tested for their inhibitory activity on the PDGF-stimulated proliferation of rat aortic vascular smooth muscle cells. Among them, 6-arylthio-5-chloro-2-phenyl-1*H*-benzo[*d*]imidazole-4,7-diones exhibited an potent antiproliferative activity.

New targeting system for antimycotic drugs: β-Glucosidase sensitive Amphotericin B–star poly(ethylene glycol) conjugate pp 2952–2956
Miloš Sedlák,* Pavel Drabina, Eliška Bílková, Petr Šimnek and Vladimír Buchta

The prepared conjugate of Amphotericin B with star poly(ethylene glycol) represent a new targeting system which is sensitive to β-glucosidases (E.C.3.2.1.21).



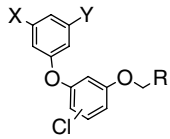
Synthesis of gemcitabine triphosphate (dFdCTP) as a tris(triethylammonium) salt pp 2957–2958
Prabhakar A. Risbood,* Charles T. Kane, Jr., Md. Tafazzal Hossain, Sudhakarrao Vadapalli and Satish K. Chadda



First synthesis of gemcitabine triphosphate (dFdCTP) as a tris(triethylammonium) salt is reported.

The design and synthesis of diaryl ether second generation HIV-1 non-nucleoside reverse transcriptase inhibitors (NNRTIs) with enhanced potency versus key clinical mutations pp 2959–2966

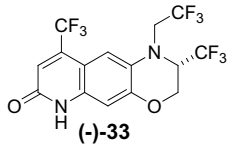
Thomas J. Tucker,* Sandeep Saggar, John T. Sisko, Robert M. Tynebor, Theresa M. Williams, Peter J. Felock, Jessica A. Flynn, Ming-Tain Lai, Yuexia Liang, Georgia McGaughey, Meiquing Liu, Mike Miller, Gregory Moyer, Vandna Munshi, Rebecca Perlow-Poehnelt, Sridhar Prasad, Rosa Sanchez, Maricel Torrent, Joseph P. Vacca, Bang-Lin Wan and Youwei Yan



The design and synthesis of novel diaryl ether NNRTIs with high levels of antiviral potency is reported.

Selective androgen receptor modulators based on a series of 7*H*-[1,4]oxazino[3,2-*g*]quinolin-7-ones with improved in vivo activity pp 2967–2971

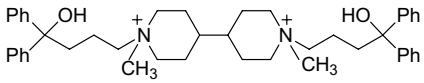
Yun Oliver Long,* Robert I. Higuchi,* Thomas R. Caferro, Thomas L. S. Lau, Min Wu, Marquis L. Cummings, Esther A. Martinborough, Keith B. Marschke, William Y. Chang, Francisco J. López, Donald S. Karanewsky and Lin Zhi



The synthesis and biological evaluation of a selective androgen receptor modulator (SARM) with improved in vivo activity is reported.

Diphenidol-related diamines as novel muscarinic M_4 receptor antagonists pp 2972–2976

Lucilla Varoli,* Aldo Andreani, Silvia Burnelli, Massimiliano Granaiola, Alberto Leoni, Alessandra Locatelli, Rita Morigi, Mirella Rambaldi, Andrea Bedini, Nicola Fazio and Santi Spampinato

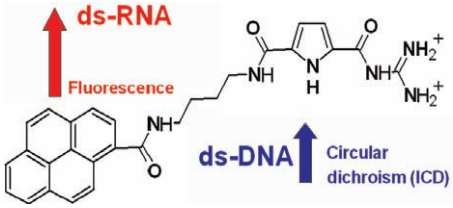


8b

The synthesis and pharmacological evaluation of novel diphenidol derivatives as muscarinic M_1–M_5 receptor antagonists are described. Compound **8b** displayed a potent and selective in vitro activity as M_4 antagonist.

A novel pyrene-guanidiniocarbonyl-pyrrole cation efficiently differentiates between ds-DNA and ds-RNA by two independent, sensitive spectroscopic methods pp 2977–2981

Laura Hernandez-Folgado, Carsten Schmuck,* Sanja Tomić and Ivo Piantanida*

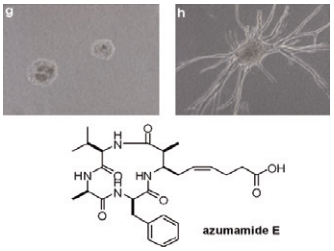


At micromolar concentrations and equimolar conditions in respect to basepairs, compound **1** exhibited strong specific ICD signal at about 300 nm for ds-DNA, and new fluorescence signal at 480 nm exclusively for ds-RNA.

Evaluation of antiangiogenic activity of azumamides by the in vitro vascular organization model using mouse induced pluripotent stem (iPS) cells pp 2982–2984

Yoichi Nakao,* Genta Narazaki, Takuhiro Hoshino, Satoko Maeda, Minoru Yoshida, Hiroshi Maejima and Jun K. Yamashita*

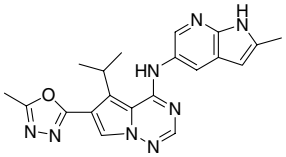
Evaluation of antiangiogenic activity of azumamide E is reported.



Discovery and preclinical studies of 5-isopropyl-6-(5-methyl-1,3,4-oxadiazol-2-yl)-*N*-(2-methyl-1*H*-pyrrolo[2,3-*b*]pyridin-5-yl)pyrrolo[2,1-*f*][1,2,4]triazin-4-amine (BMS-645737), an in vivo active potent VEGFR-2 inhibitor pp 2985–2989

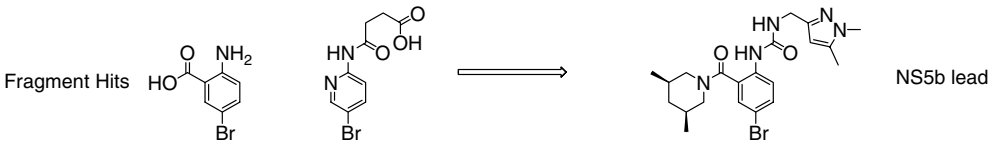
Réjean Ruel,* Carl Thibeault, Alexandre L'Heureux, Alain Martel, Zhen-Wei Cai, Donna Wei, Ligang Qian, Joel C. Barrish, Arvind Mathur, Celia D'Arienzo, John T. Hunt, Amrita Kamath, Punit Marathe, Yueping Zhang, George Derbin, Barri Wautlet, Steven Mortillo, Robert Jeyaseelan, Sr., Benjamin Henley, Ravindra Tejwani, Rajeev S. Bhide, George L. Trainor, Joseph Fargnoli and Louis J. Lombardo

We report herein a series of substituted *N*-(1*H*-pyrrolo[2,3-*b*]pyridin-5-yl)pyrrolo[2,1-*f*][1,2,4]triazin-4-amines as inhibitors of vascular endothelial growth factor receptor-2 tyrosine kinase. Through structure–activity relationship studies, biochemical potency, pharmacokinetics, and kinase selectivity were optimized to afford BMS-645737 (**13**), a compound with good preclinical in vivo activity against human tumor xenograft models.



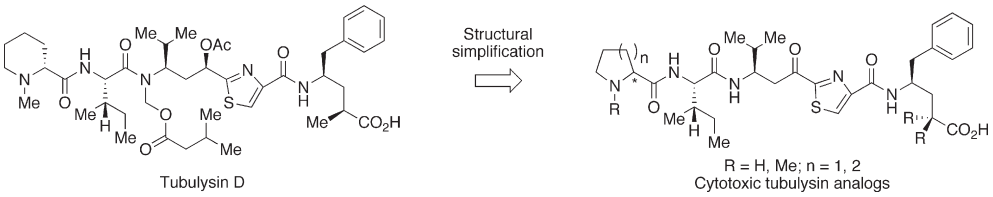
Fragment-based discovery of hepatitis C virus NS5b RNA polymerase inhibitors pp 2990–2995

Stephen S. Antonysamy, Brandon Aubol, Jeff Blaney, Michelle F. Browner, Anthony M. Giannetti, Seth F. Harris, Normand Hébert,* Jörg Hendle, Stephanie Hopkins, Elizabeth Jefferson, Charles Kissinger, Vincent Leveque, David Marciano, Ethel McGee, Isabel Nájera, Brian Nolan, Masaki Tomimoto, Eduardo Torres and Tobi Wright



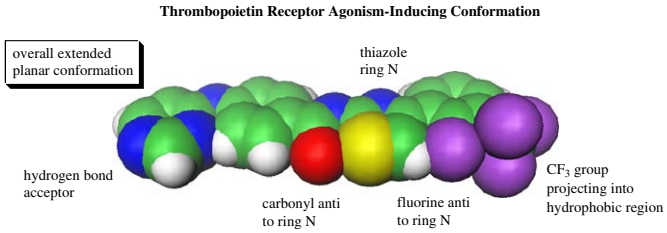
Tubulysin analogs incorporating desmethyl and dimethyl tubuphenylalanine derivatives pp 2996–2999

Ranganathan Balasubramanian, Bhooma Raghavan, Jaeson C. Steele, Dan L. Sackett and Robert A. Fecik*



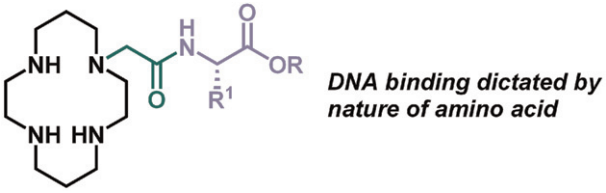
Molecular features crucial to the activity of pyrimidine benzamide-based thrombopoietin receptor agonists **pp 3000–3006**

Lawrence A. Reiter, Christopher S. Jones,* William H. Brissette, Sandra P. McCurdy, Yuriy A. Abramov,* Jon Bordner, Frank M. DiCapua, Michael J. Munchhof, Diane M. Rescek, Ivan J. Samardjiev and Jane M. Withka



Synthesis and DNA binding ability of cyclam–amino acid conjugates **pp 3007–3010**

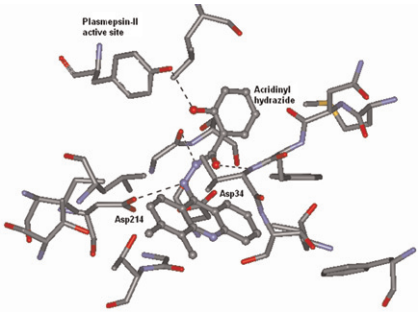
A. Venkata Ramana, Michael Watkinson and Matthew H. Todd*



Identification of acridinyl hydrazides as potent aspartic protease inhibitors **pp 3011–3015**

M. Kamran Azim,* Waseem Ahmed, Ishtiaq A. Khan, Nosheen A. Rao and Khalid M. Khan

Docking of acridinyl hydrazides in the substrate-binding cleft of plasmepsin-II from *Plasmodium falciparum*.



OTHER CONTENTS

Summary of instructions to authors **p I**

*Corresponding author

Supplementary data available via ScienceDirect

COVER

Overlay of a recolored light microscopic photograph view of a male *Nematodirus spathiger* nematode and the X-ray structure of compound (*S*)-36 a potent member of a new class of synthetic anthelmintics: the amino-acetonitrile derivatives (AAD). [Ducray, P.; Gauvry, N.; Pautrat, F.; Goebel, T.; Fruechtel, J.; Desaules, Y.; Schorderet Weber, S.; Bouvier, J.; Wagner, T.; Froelich, O.; Kaminsky, R. *Bioorg. Med. Chem. Lett.* **2008**, *18,* 2935.]

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