

Contents

Publisher's Note

p 4650

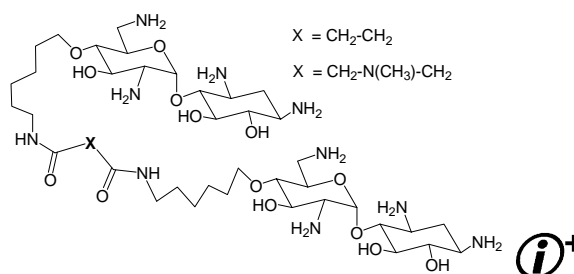
ARTICLES

Neamine dimers targeting the HIV-1 TAR RNA

pp 4651–4655

Emmanuel Riguet, Jérôme Désiré, Oliver Boden, Verena Ludwig, Michael Göbel, Christian Bailly and Jean-Luc Décout*

The natural antibiotic agent neomycin binds strongly to HIV TAR RNA through the predominant interactions of its neamine core and inhibits the TAR-Tat protein association necessary for viral RNA transactivation. In the search for new antiviral agents, neamine dimers were found to be able to inhibit the TAR-Tat association, with IC_{50} values 17–85 times better than that obtained with neomycin.

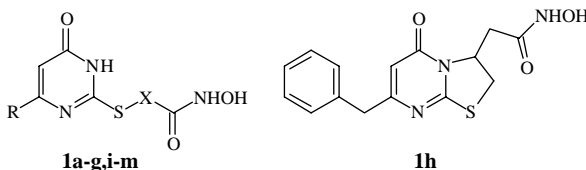


Exploring the connection unit in the HDAC inhibitor pharmacophore model:

pp 4656–4661

Novel uracil-based hydroxamates

Antonello Mai,* Silvio Massa, Dante Rotili, Riccardo Pezzi, Patrizia Bottoni, Roberto Scatena, Joachim Meraner and Gerald Brosch*



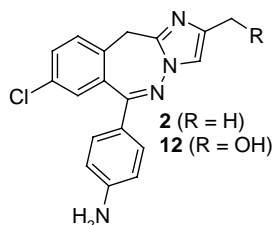
R = H, Me, n-Pr, Ph, Bz, 2-Ph-ethyl
X = CH=CH, (CH₂)_n, n = 2–7

i+

Potential metabolites of a condensed 2,3-benzodiazepine derivative

pp 4662–4665

Emese Csuzdi, Katalin Miglécz, István Hazai, Pál Berzsenyi, István Pallagi, Gyula Horváth, György Lengyel and Sándor Sólyom*



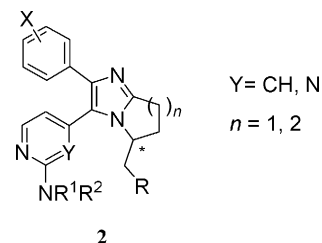
Putative metabolites of **2** were synthesized and compared to constituents formed in an ex vivo rat liver perfusion experiment.

The neuroprotective action of JNK3 inhibitors based on the 6,7-dihydro-5H-pyrrolo[1,2-a]imidazole scaffold

pp 4666–4670

Piotr P. Graczyk,* Afzal Khan, Gurpreet S. Bhatia, Vanessa Palmer, Darren Medland, Hirotoshi Numata, Hitoshi Oinuma, Jacqueline Catchick, Angela Dunne, Moira Ellis, Caroline Smales, Jonathan Whitfield, Stephen J. Neame, Bina Shah, Daniel Wilton, Louise Morgan, Toshali Patel, Raymond Chung, Howard Desmond, James M. Staddon, Nobuaki Sato and Atsushi Inoue

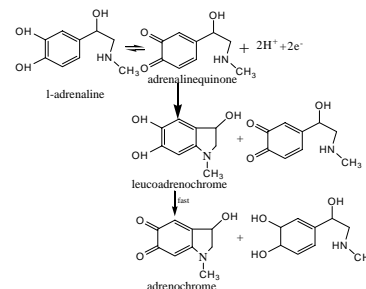
The synthesis and neuroprotective properties of three representative enantiomeric pairs (*S*)-**2** and (*R*)-**2** are reported.


Density-functional theory studies on standard electrode potentials of half reaction for L-adrenaline and adrenalinequinone

pp 4671–4680

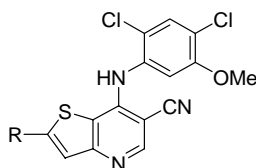
Yuanzhi Song,* JianFeng Zhou, Yang Song, Yongge Wei and Hong Wang

Cyclic voltammetry with a platinum electrode of L-adrenaline solutions in phosphate buffers at pH 1 shows that standard electrode potential of half reaction for L-adrenaline and adrenalinequinone is 0.803 V. The predicted standard electrode potentials of 0.57 V at B3LYP/6-31G(d) level and 0.67 V at B3PW91/6-31G(d) level for L-adrenaline and adrenalinequinone are in better agreement with experimental data. This method is very useful for predicting unknown standard potential of compounds.


Inhibition of Src kinase activity by 7-[(2,4-dichloro-5-methoxyphenyl)amino]-2-heteroaryl-thieno[3,2-b]pyridine-6-carbonitriles

pp 4681–4684

Diane H. Boschelli,* Biqi Wu, Ana Carolina Barrios Sosa, Joan J. Chen, Jennifer M. Golas and Frank Boschelli

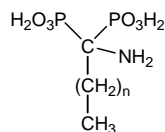


7-[(2,4-Dichloro-5-methoxyphenyl)amino]thieno[3,2-b]pyridine-6-carbonitriles with various heteroaryl groups at C-2 are inhibitors of Src kinase activity.

Synthesis and biological evaluation of 1-amino-1,1-bisphosphonates derived from fatty acids against *Trypanosoma cruzi* targeting farnesyl pyrophosphate synthase

pp 4685–4690

Sergio H. Szajnman, Esteban L. Ravaschino, Roberto Docampo and Juan B. Rodriguez*

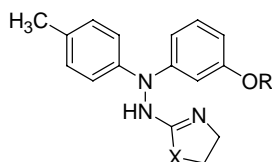


1-Amino-1,1-bisphosphonates derived from fatty acids were shown to be potent inhibitors of *Trypanosoma cruzi* farnesyl pyrophosphate synthase activity.

Bioisosteric phentolamine analogs as potent α -adrenergic antagonists

pp 4691–4695

Seoung-Soo Hong,* Supriya A. Bavadekar, Sang-Il Lee, Popat. N. Patil,
S. G. Lalchandani, Dennis R. Feller and Duane D. Miller

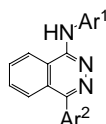


The synthesis and biological evaluation of a new series of bioisosteric phentolamine analogs are described.

Arylphthalazines: Identification of a new phthalazine chemotype as inhibitors of VEGFR kinase

pp 4696–4698

Evgueni L. Piatnitski, Matthew A. J. Duncton,* Alexander S. Kiselyov,
Reeti Katoch-Rouse, Dan Sherman, Daniel L. Milligan, Chris Balagtas,
Wai C. Wong, Joel Kawakami and Jacqueline F. Doody



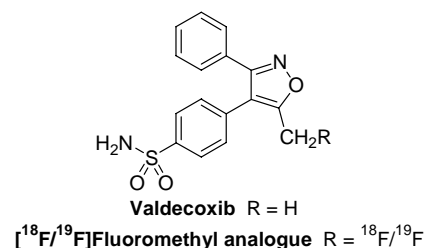
The synthesis and structure–activity relationships for a new class of arylphthalazine derivatives, which have found use as inhibitors of VEGFR-2 kinase, are reported.

Synthesis of 4-(5-[18 F]fluoromethyl-3-phenylisoxazol-4-yl)benzenesulfonamide, a new [18 F]fluorinated analogue of valdecocix, as a potential radiotracer for imaging cyclooxygenase-2 with positron emission tomography

pp 4699–4702

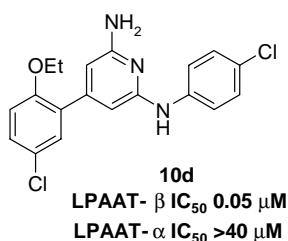
Tatsushi Toyokuni,* J. S. Dileep Kumar, Joseph C. Walsh,
Alan Shapiro, John J. Talley, Michael E. Phelps, Harvey R. Herschman,
Jorge R. Barrio and Nagichettiar Satyamurthy

The [18 F]fluoromethyl analogue of valdecocix (~2000 Ci/mmol) was synthesized by [18 F]fluoride-ion displacement of the corresponding tosylate in ~40% decay-corrected radiochemical yield within ~120 min from end of bombardment.

**Diamino-*C,N*-diarylpyridine positional isomers as inhibitors of lysophosphatidic acid acyltransferase- β**

pp 4703–4707

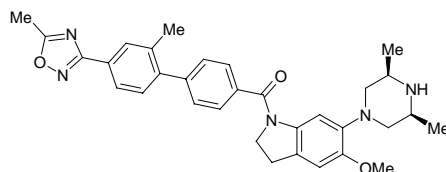
Feng Hong, David Hollenback, Jack W. Singer and Peter Klein*



Identification of a potent and selective 5-HT_{1B} receptor antagonist

pp 4708–4712

Paul A. Wyman,* Howard R. Marshall, Sean T. Flynn, Ron J. King, Mervyn Thompson, Paul W. Smith, Michael S. Hadley, Gary W. Price, Claire M. Scott and Lee A. Dawson



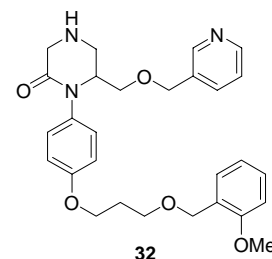
Introduction of *cis*-2,6-dimethyl substitution onto the piperazine ring of a mixed 5-HT_{1ABD} receptor antagonist offers a combination of both excellent selectivity over 5-HT_{1A} and 5-HT_{1D} receptors and low intrinsic activity.

Benzyl ether structure–activity relationships in a series of ketopiperazine-based renin inhibitors

pp 4713–4716

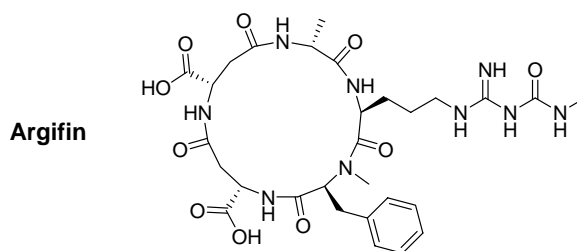
Noel A. Powell,* Emma H. Clay, Daniel D. Holsworth, John W. Bryant, Michael J. Ryan, Mehran Jalaie and Jeremy J. Edmunds

Inhibition of renin enzymatic activity by a series of ketopiperazine-based compounds containing a C6 benzyloxymethyl substituent correlated with a $+(\pi+\sigma)$ effect. A 3-pyridinyloxymethyl substituent was also found to be equipotent as higher molecular weight analogs, and exhibited decreased CYP3A4 inhibition levels and improved pharmacokinetic properties.

**An efficient synthesis of argifin: A natural product chitinase inhibitor with chemotherapeutic potential**

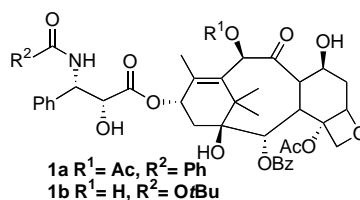
pp 4717–4721

Mark J. Dixon, Ole A. Andersen, Daan M. F. van Aalten and Ian M. Eggleston*

**Novel C2–C3' N-peptide linked macrocyclic taxoids. Part 1: Synthesis and biological activities of docetaxel analogues with a peptide side chain at C3'**

pp 4722–4726

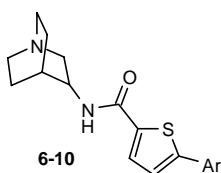
Anne-Laure Larroque, Joëlle Dubois, Sylviane Thoret, Geneviève Aubert, Daniel Guénard and Françoise Guéritte*



The synthesis and biological activities of docetaxel analogues possessing a peptide side chain at the C3'-N position are described. The chosen amino acids are part of the α -tubulin loop that is equivalent to the paclitaxel binding pocket in β -tubulin.

High affinity ligands for the $\alpha 7$ nicotinic receptor that show no cross-reactivity with the 5-HT₃ receptor pp 4727–4730

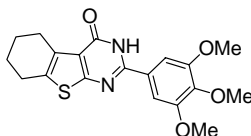
S. Richard Baker, John Boot, Michael Brunavs, David Dobson, Rachel Green,
Lorna Hayhurst, Martine Keenan* and Louise Wallace



Certain quinuclidine 3-biarylcarboxamides are high affinity nicotinic $\alpha 7$ ligands with an excellent binding selectivity over the 5-HT₃ receptor.

Parallel synthesis and biological evaluation of 5,6,7,8-tetrahydrobenzothieno[2,3-*d*]pyrimidin-4(3H)-one pp 4731–4735

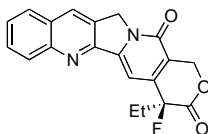
Lee D. Jennings,* Scott L. Kincaid, Yanong D. Wang, Girija Krishnamurthy, Carl F. Beyer,
John P. McGinnis, Miriam Miranda, Carolyn M. Discafani and Sridhar K. Rabindran



A novel series of anti-proliferative agents containing the thieno[2,3-*d*]pyrimidin-4-one scaffold and the structure–activity relationship studies to improve potency is described.

Total and semisynthesis and in vitro studies of both enantiomers of 20-fluorocamptothecin pp 4736–4740

Raghuram S. Tangirala, Rachel Dixon, Danzhou Yang, Attila Ambrus, Smitha Antony, Keli Agama,
Yves Pommier and Dennis P. Curran*

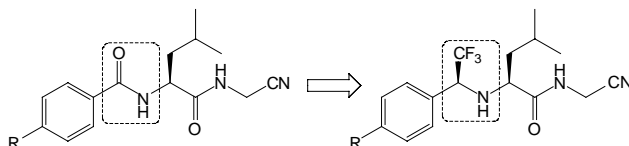


Both enantiomers of 20-fluorocamptothecin and the racemate have been prepared by total synthesis. The (*R*)-enantiomer is essentially inactive in a topoisomerase-I/DNA assay, while the (*S*)-enantiomer is much less active than 20(*S*)-camptothecin. The lactone ring of 20-fluorocamptothecin hydrolyzes more rapidly than that of camptothecin in PBS.

**Trifluoroethylamines as amide isosteres in inhibitors of cathepsin K**

pp 4741–4744

W. Cameron Black,* Christopher I. Bayly, Dana E. Davis, Sylvie Desmarais,
Jean-Pierre Falgout, Serge Léger, Chun Sing Li, Frédéric Massé, Daniel J. McKay,
James T. Palmer, M. David Percival, Joël Robichaud, Nancy Tsou and Robert Zamboni

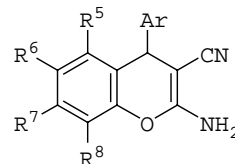


Replacing an amide bond with a trifluoroethylamine leads to potent and selective inhibitors of cathepsin K. The CF₃ group provides a non-basic amine that makes a good hydrogen bond with the enzyme active site.

Discovery of 4-aryl-4*H*-chromenes as a new series of apoptosis inducers using a cell- and caspase-based high-throughput screening assay. 2. Structure–activity relationships of the 7- and 5-, 6-, 8-positions

William Kemnitzer, Shailaja Kasibhatla, Songchun Jiang, Hong Zhang, Jianghong Zhao, Shaojuan Jia, Lifan Xu, Candace Crogan-Grundy, Réal Denis, Nancy Barriault, Louis Vaillancourt, Sylvie Charron, Jennifer Dodd, Giorgio Attardo, Denis Labrecque, Serge Lamothe, Henriette Gourdeau, Ben Tseng, John Drewe and Sui Xiong Cai*

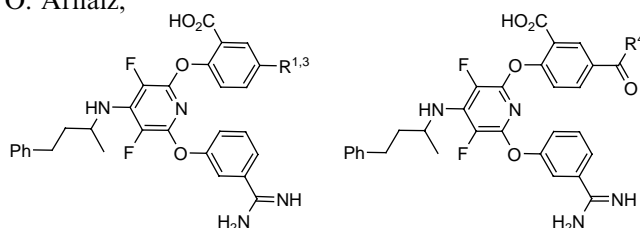
The synthesis and SAR of a group of apoptosis inducing 4-aryl-4*H*-chromenes with modifications at the 7- and 5-, 6-, 8-positions are reported.



The discovery of fluoropyridine-based inhibitors of the Factor VIIa/TF complex

pp 4752–4756

Jeffrey T. Kohrt,* Kevin J. Filipinski, Wayne L. Cody, Cuiman Cai, Danette A. Dudley, Chad A. Van Huis, J. Adam Willardsen, Stephen T. Rapundalo, Kamlai Saiya-Cork, Robert J. Leadley, Lakshmi Narasimhan, Erli Zhang, Marc Whitlow, Marc Adler, Kirk McLean, Yuo-Ling Chou, Cecile McKnight, Damian O. Arnaiz, Kenneth J. Shaw, David R. Light and Jeremy J. Edmunds

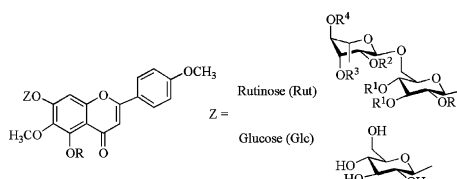


Potential antitumor agents: Flavones and their derivatives from *Linaria reflexa* Desf.

pp 4757–4760

Rosa Tundis,* Brigitte Deguin, Monica R. Loizzo, Marco Bonesi, Giancarlo A. Statti, François Tillequin and Francesco Menichini

Compounds	Z	R	R ¹	R ²	R ³	R ⁴
Pectolinarin	Rut	H	H	H	H	H
Linariin	Rut	H	H	H	H	Ac
Isolinarin A	Rut	H	H	Ac	H	H
Isolinarin B	Rut	H	H	H	Ac	H
Pectolinarigenin-7-O-β-glc	Glc	H	/	/	/	/
Pectolinarigenin	H	H	/	/	/	/
Peracetylpectolinarin	Rut	Ac	Ac	Ac	Ac	Ac



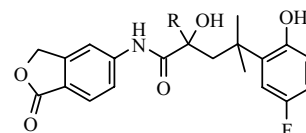
The antiproliferative activity of several flavonoids isolated for the first time from *Linaria reflexa* Desf. and their derivatives was evaluated in vitro by the SRB assay against the tumor cell lines Caco-2, COR-L23, HepG-2, ACHN, C32, and normal cell line MRC5.

Trifluoromethyl group as a pharmacophore: Effect of replacing a CF₃ group on binding and agonist activity of a glucocorticoid receptor ligand

pp 4761–4769

Raj Betageri,* Yan Zhang, Renee M. Zindell, Daniel Kuzmich, Thomas M. Kirrane, Jörg Bentzien, Mario Cardozo, Alison J. Capolino, Tazmeen N. Fadra, Richard M. Nelson, Zofia Paw, Daw-Tsun Shih, Cheng-Kon Shih, Ljiljana Zuvela-Jelaska, Gerald Nabozny and David S. Thomson

SAR describing the effect of replacing the trifluoromethyl group and modifying other parts of the glucocorticoid receptor ligand (R = CF₃) on binding and agonist activity are presented.

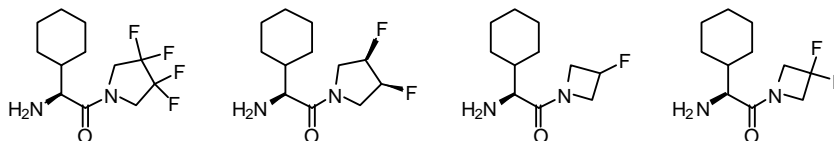


R = CF₃, benzyl and cyclohexylmethyl

New fluorinated pyrrolidine and azetidine amides as dipeptidyl peptidase IV inhibitors

pp 4770–4773

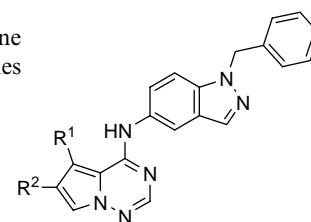
Bernard Hulin,* Shawn Cabral, Michael G. Lopaze, Maria A. Van Volkenburg, Kim M. Andrews and Janice C. Parker

**New dual inhibitors of EGFR and HER2 protein tyrosine kinases**

pp 4774–4779

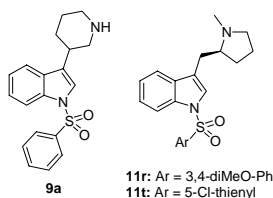
Brian E. Fink,* Gregory D. Vite, Harold Mastalerz, John F. Kadow, Soong-Hoon Kim, Kenneth J. Leavitt, Karen Du, Donald Crews, Toomas Mitt, Tai W. Wong, John T. Hunt, Dolatrai M. Vyas and John S. Tokarski

A novel series of dual EGFR and HER2 inhibitors based on the pyrrolo[2,1-*f*][1,2,4]triazine nucleus is described. Biological evaluation in enzymatic and cell-based assays has identified a series of C-6 carbamates with potent biochemical and cellular activities.

**Conformationally constrained *N*₁-arylsulfonyltryptamine derivatives as 5-HT₆ receptor antagonists**

pp 4780–4785

Derek C. Cole,* William J. Lennox, Joseph R. Stock, John W. Ellingboe, Hossein Mazandarani, Deborah L. Smith, Guoming Zhang, Gregory J. Tawa and Lee E. Schechter

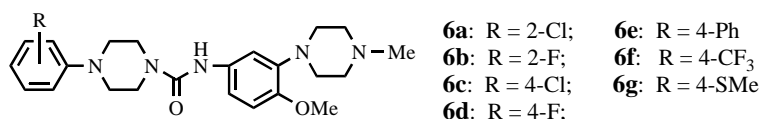


The discovery of *N*₁-arylsulfonyl-3-piperidin-3-yl-, -3-(1-methylpyrrolidin-2-ylmethyl)-, and -3-pyrrolidin-3-yl-1*H*-indoles as high affinity 5-HT₆ receptor ligands is described. *N*₁-Benzenesulfonyl-3-piperidin-3-yl-1*H*-indole **9a** is a 24 nM full agonist, while *N*₁-arylsulfonyl-3-(1-methylpyrrolidin-2-ylmethyl)-1*H*-indole derivatives **11r** and **11t** behave as very potent antagonists.

Synthesis of potent and selective serotonin 5-HT_{1B} receptor ligands

pp 4786–4789

Yiyun Huang,* Sung-A Bae, Bryan L. Roth and Marc Laruelle

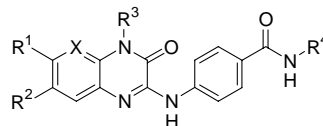


A series of serotonin 5-HT_{1B} ligands were synthesized and evaluated for their potency and selectivity against other 5-HT receptor subtypes. Many of these new compounds displayed high affinity and selectivity for the 5-HT_{1B} receptor and compound **6c** was found to have the in vitro binding profile necessary for development as a PET radioligand.

Synthesis and evaluation of 3-anilino-quinoxalinones as glycogen phosphorylase inhibitors

pp 4790–4793

Joseph Dudash, Jr.,* Yongzheng Zhang, John B. Moore, Richard Look, Yin Liang, Mary Pat Beavers, Bruce R. Conway, Philip J. Rybczynski and Keith T. Demarest

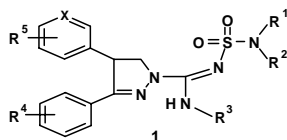


A series of 3-anilino-quinoxalinones has been identified as a new class of glycogen phosphorylase inhibitors.

Novel 3,4-diarylpyrazolines as potent cannabinoid CB₁ receptor antagonists with lower lipophilicity

pp 4794–4798

Jos H. M. Lange,* Herman H. van Stuivenberg, Willem Veerman, Henri C. Wals, Bob Stork, Hein K. A. C. Coolen, Andrew C. McCreary, Tiny J. P. Adolfs and Chris G. Kruse

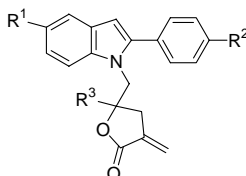


Novel 3,4-diaryldihydropyrazoles **1** as potent CB₁ receptor antagonists with lower lipophilicity are described. The key change is the replacement of the arylsulfonyl group in the original series by a dialkylaminosulfonyl moiety.

Novel indole α -methylene- γ -lactones as potent inhibitors for AKT-mTOR signaling pathway kinases

pp 4799–4802

Huasheng Ding, Chao Zhang, Xihan Wu, Chunhao Yang,* Xiongwen Zhang, Jian Ding and Yuyuan Xie

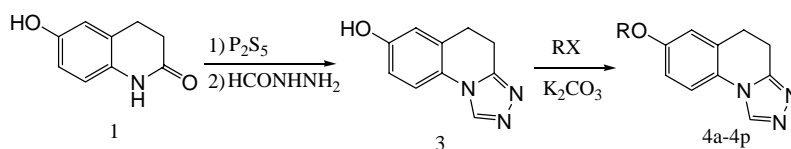


A novel series of indole α -methylene- γ -lactones with remarkable inhibition ability on phosphorylation of AKT, mTOR, p70S6 kinase, and 4E-BP1 has been synthesized.

Synthesis and anticonvulsant activity of 7-alkoxyl-4,5-dihydro-[1,2,4]triazolo[4,3-*a*]quinolines

pp 4803–4805

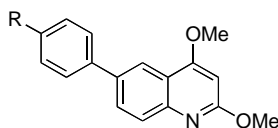
Zhi-Feng Xie, Kyu-Yun Chai, Hu-Ri Piao, Kyung-Chell Kwak and Zhe-Shan Quan*



A series of new 7-alkoxyl-4,5-dihydro-[1,2,4]triazolo[4,3-*a*]quinolines has been synthesized and evaluated as anticonvulsant agents. The MES and scMet tests show that 7-(4-fluorobenzoyloxy)-4,5-dihydro-[1,2,4]triazolo[4,3-*a*]quinoline **4l** was found to be the most potent, with ED₅₀ values of 11.8 and 6.7 mg kg⁻¹, respectively.

Synthesis and anthelmintic properties of arylquinolines with activity against drug-resistant nematodes pp 4806–4808

Sharon Rossiter, Jean-Marie Péron, Philip J. Whitfield and Keith Jones*

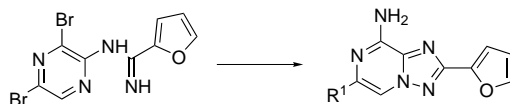


A number of aryl-substituted 2,4-dimethoxyquinolines have been synthesized and tested against a range of nematodes. The 6-substituted compounds show significant activity against resistant strains.

Synthesis of [1,2,4]triazolo[1,5-*a*]pyrazines as adenosine A_{2A} receptor antagonists

pp 4809–4813

James E. Dowling,* Jeffrey T. Vessels, Serajul Haque, He Xi Chang, Kurt van Vloten, Gnanasambandam Kumaravel, Thomas Engber, Xiaowei Jin, Deepali Phadke, Joy Wang, Eman Ayyub and Russell C. Petter

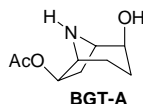


This paper describes the preparation, by a novel route, of A_{2A} receptor antagonists containing the [1,2,4]triazolo[1,5-*a*]pyrazine nucleus, which is isomeric with the [1,2,4]triazolo[1,5-*c*]pyrimidine core of a series of known A_{2A} antagonists with in vivo activity in animal models of Parkinson's disease.

Activity and QSAR study of baogongteng A and its derivatives as muscarinic agonists

pp 4814–4818

Yin-Yao Niu, Li-Min Yang, Hui-Zhong Liu, Yong-Yao Cui, Liang Zhu, Ju-Mei Feng, Jian-Hua Yao, Hong-Zhuan Chen, Bo-Tao Fan, Ze-Nai Chen and Yang Lu*

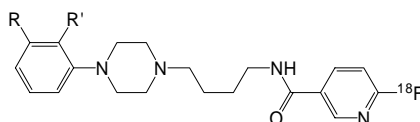


A new CoMFA model of baogongteng A (BGT-A) and its derivatives with agonistic activity to muscarinic receptors was constructed, discussed, and examined. This model could provide solid basis for designing novel molecules with higher agonistic activity to muscarinic receptors.

Synthesis and evaluation of ¹⁸F-labeled dopamine D3 receptor ligands as potential PET imaging agents

pp 4819–4823

Carsten Hocke,* Olaf Prante, Stefan Löber, Harald Hübner, Peter Gmeiner and Torsten Kuwert

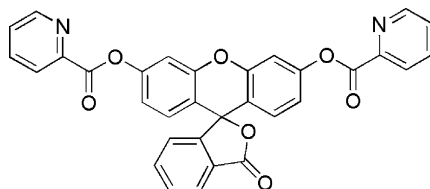


A series of dopamine D3 receptor radioligands were synthesized. The 6-fluoropyridin-3-yl derivative [¹⁸F]**8d** displayed good D3 affinity (*K*_i = 1.1 nM) and was used for receptor autoradiography studies on rat brain slices.

A fluorogenic and chromogenic probe that detects the esterase activity of trace copper(II)

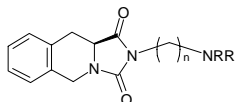
pp 4824–4827

Radoslaw M. Kierat and Roland Krämer*

**Synthesis and pharmacological evaluation of Tic-hydantoin derivatives as selective σ_1 ligands. Part 2**

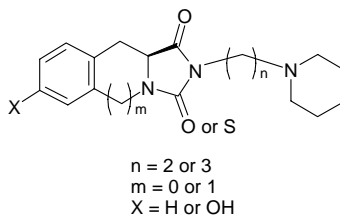
pp 4828–4832

Amaury Cazenave Gassiot, Julie Charton, Sophie Girault-Mizzi, Pauline Gilleron, Marie-Ange Debreu-Fontaine, Christian Sergheraert and Patricia Melnyk*

**Synthesis and pharmacological evaluation of Tic-hydantoin derivatives as selective σ_1 ligands. Part 1**

pp 4833–4837

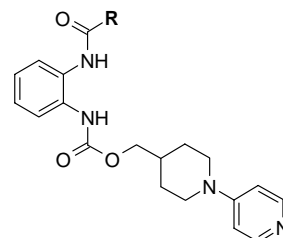
Julie Charton, Amaury Cazenave Gassiot, Sophie Girault-Mizzi, Marie-Ange Debreu-Fontaine, Patricia Melnyk* and Christian Sergheraert

**Investigation of factor Xa inhibitors containing non-amidine S1 elements**

pp 4838–4841

Jeffrey B. Franciskovich,* John J. Masters, Jennifer M. Tinsley, Trelia J. Craft, Larry L. Froelich, Donetta S. Gifford-Moore, Valentine J. Klimkowski, Jeffrey K. Smallwood, Gerald F. Smith, Tommy Smith, Richard R. Towner, Leonard C. Weir and Michael R. Wiley

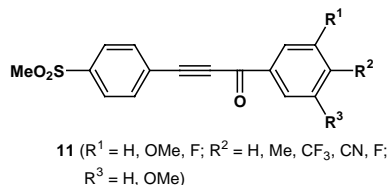
Several non-amidino S1 derivatives of the 1,2-diaminobenzene-based scaffold were synthesized and evaluated for their ability to inhibit the human protease factor Xa.



Synthesis and biological evaluation of 1,3-diphenylprop-2-yn-1-ones as dual inhibitors of cyclooxygenases and lipxygenases

pp 4842–4845

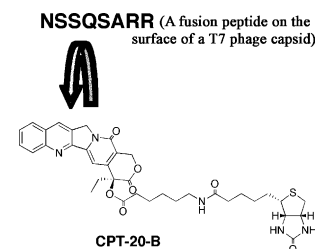
P. N. Praveen Rao, Qiao-Hong Chen and Edward E. Knaus*

**Synthesis of a biotinylated camptothecin derivative and determination of the binding sequence by T7 phage display technology**

pp 4846–4849

Yoichi Takakusagi, Keisuke Ohta, Kouji Kuramochi, Kengo Morohashi, Susumu Kobayashi, Kengo Sakaguchi and Fumio Sugawara*

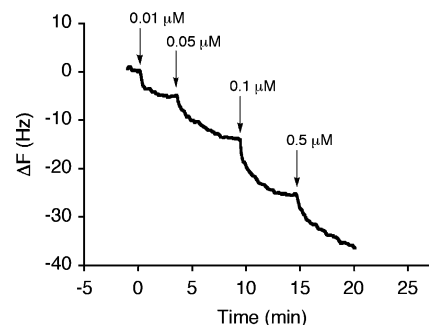
Synthesis of CPT-20-B and peptide screening by T7 phage display method have been reported.

**Camptothecin binds to a synthetic peptide identified by a T7 phage display screen**

pp 4850–4853

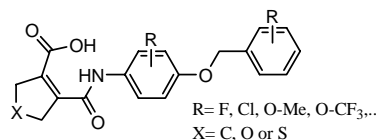
Yoichi Takakusagi, Susumu Kobayashi* and Fumio Sugawara*

An analysis of non-biotinylated camptothecin (CPT) binding to the C-20-biotinylated CPT binding peptide was carried out using QCM and SPR.

**SAR, species specificity, and cellular activity of cyclopentene dicarboxylic acid amides as DHODH inhibitors**

pp 4854–4857

Johann Leban,* Martin Kralik, Jan Mies, Michael Gassen, Karin Tentschert and Roland Baumgartner

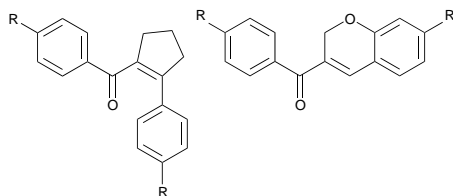


Novel DHODH inhibitors were developed, based on a previously described series by introduction of heteroatoms into the cyclopentene ring and hydroxyl groups attached to it. Also, the hydrophobic biphenyl side chain was replaced with benzyloxy phenyl groups. Activities on human, rat, and mouse enzymes indicate a species specificity of these inhibitors.

Conformationally restricted anti-plasmodial chalcones

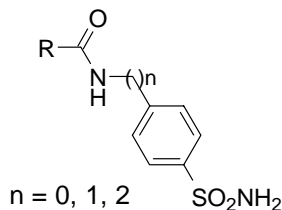
pp 4858–4861

Mogens Larsen, Hasse Kromann, Arsalan Kharazmi and Simon Feldbæk Nielsen*

**Carbonic anhydrase inhibitors: Inhibition of the tumor-associated isozymes IX and XII with a library of aromatic and heteroaromatic sulfonamides**

pp 4862–4866

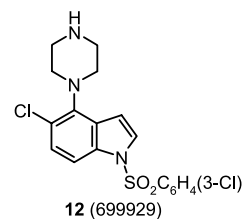
Özen Özensoy, Luca Puccetti, Giuseppe Fasolis, Oktay Arslan, Andrea Scozzafava and Claudiu T. Supuran *

**Bicyclic heteroaryl piperazines as selective brain penetrant 5-HT₆ receptor antagonists**

pp 4867–4871

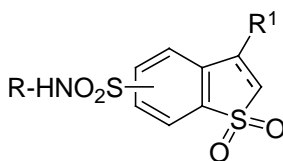
Mahmood Ahmed, Michael A. Briggs, Steven M. Bromidge, Tania Buck, Lorraine Campbell, Nigel J. Deeks, Ashley Garner, Laurie Gordon, Dieter W. Hamprecht, Vicky Holland, Christopher N. Johnson,* Andrew D. Medhurst, Darren J. Mitchell, Stephen F. Moss, Jenifer Powles, Jon T. Seal, Tania O. Stean, Geoffrey Stemp, Mervyn Thompson, Brenda Trail, Neil Upton, Kim Winborn and David R. Witty

The selective, brain penetrant and orally bioavailable 5-HT₆ receptor antagonist **12** (699929) is described.

**Carbonic anhydrase inhibitors: Inhibition of cytosolic/tumor-associated carbonic anhydrase isozymes I, II, and IX with benzo[*b*]thiophene 1,1-dioxide sulfonamides**

pp 4872–4876

Alessio Innocenti, Raquel Villar, Victor Martinez-Merino, María J. Gil, Andrea Scozzafava, Daniela Vullo and Claudiu T. Supuran*



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*Corresponding author

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

Amerliorating transthyretin amyloidogenesis by native state kinetic stabilization mediated by small molecule binding. Small molecule binding to the amyloidogenic protein transthyretin kinetically stabilizes the native tetrameric state, preventing dissociation to folded monomers that misfold and misassemble into toxic intermediates, amorphous aggregates, and amyloid fibrils. The Kelly laboratory has developed several structurally distinct inhibitor families, depicted in the background, that are undergoing pharmacological evaluation. Created by Steven M. Johnson, graduate student in Professor Jeffery W. Kelly's laboratory, Department of Chemistry, The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA.



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