

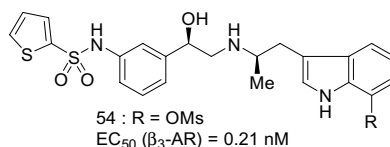
Contents

Publisher's Announcement—Chairman of the Executive Board of Editors for Tetrahedron Publications p 5957

COMMUNICATIONS

Tryptamine-based human β_3 -adrenergic receptor agonists. Part 1: SAR studies of the 7-position of the indole ring pp 5959–5962

Kazuhiro Mizuno,* Masaaki Sawa, Hiroshi Harada, Hirotaka Tateishi, Mayumi Oue, Hiroshi Tsujiuchi, Yasuji Furutani and Shiro Kato

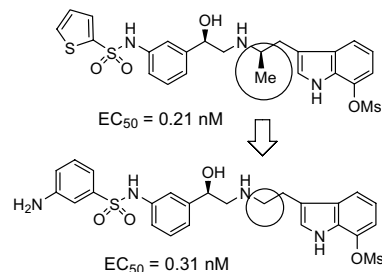


The synthesis and biological evaluation of a series of tryptamine-based β_3 -adrenergic receptor (AR) agonists are described. The methanesulfonate **54** exhibited strong agonistic activity and excellent subtype selectivity for the β_3 -AR.

Tryptamine-based human β_3 -adrenergic receptor agonists. Part 2: SAR of the methylene derivatives pp 5963–5966

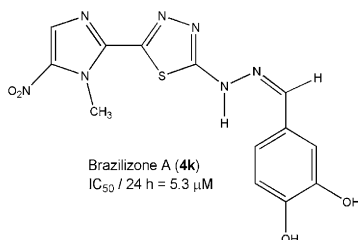
Masaaki Sawa,* Hirotaka Tateishi, Kazuhiro Mizuno, Hiroshi Harada, Mayumi Oue, Hiroshi Tsujiuchi, Yasuji Furutani and Shiro Kato

In an effort to reduce the cost of production, we conducted further optimization of tryptamine-based β_3 -adrenergic receptor (AR) agonists. Optimization of the left-hand side aryl moiety led to the identification of a series of potent β_3 -agonists without costly chiral methyl group.



Synthesis and antitrypanosomal profile of new functionalized 1,3,4-thiadiazole-2-arylhydrazones derivatives, designed as non-mutagenic megazol analogues pp 5967–5970

Samir A. Carvalho, Edson F. da Silva, Ricardo M. Santa-Rita, Solange L. de Castro and Carlos A. M. Fraga*

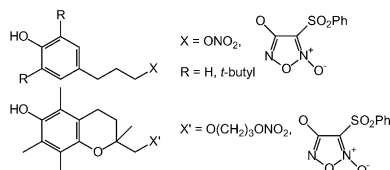


The synthesis of the new powerful trypanocidal agent brazilizone A (**4k**) (IC₅₀/24 h = 5.3 μ M) is reported.

Development of a new class of potential antiatherosclerosis agents: NO-donor antioxidants

pp 5971–5974

Clara Cena, Donatella Boschi, Gian Cesare Tron, Kostantin Chegaev, Loretta Lazzarato, Antonella Di Stilo, Manuela Aragno, Roberta Fruttero and Alberto Gasco*



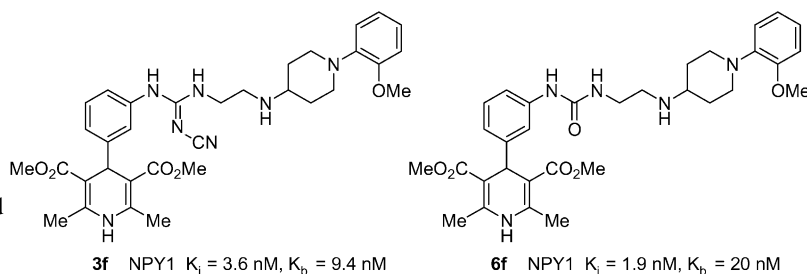
A new class of NO-donor phenol derivatives is described. The products were obtained by joining appropriate phenols with either nitrooxy or 3-phenylsulfonylfuroxan-4-yloxy moieties. All the compounds proved to inhibit the ferrous salt/ascorbate induced lipidic peroxidation of membrane lipids of rat hepatocytes. They were also capable of dilating rat aorta strips precontracted with phenylephrine.

Isosteric *N*-arylpiperazine replacements in a series of dihydropyridine NPY₁ receptor antagonists

pp 5975–5978

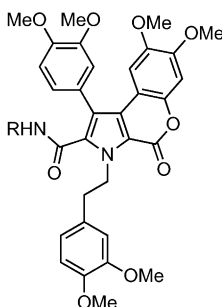
Guanglin Luo,* Gail K. Mattson, Marc A. Bruce, Henry Wong, Brian J. Murphy, Daniel Longhi, Ildiko Antal-Zimanyi and Graham S. Poindexter

4-Amino-*N*-arylpiperidines serve as effective bioisosteres for *N*-arylpiperazines in the series of dihydropyridine NPY₁ receptor antagonists. These were prepared by a ZnCl₂-mediated reductive amination reaction between elaborated primary amines and 4-arylpiperidones.

**Multidrug resistance reversal activity of permethyl ningalin B amide derivatives**

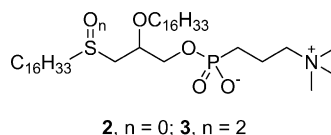
pp 5979–5981

Houchao Tao, Inkyu Hwang and Dale L. Boger*

**Synthesis and interfacial behavior of sulfur-containing analogs of lung surfactant dipalmitoyl phosphatidylcholine**

pp 5983–5986

Yusuo Chang, Zhengdong Wang, Robert H. Notter, Zhongyi Wang, Long Qu and Adrian L. Schwan*

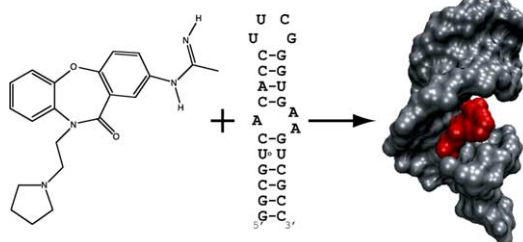


The synthesis and potential of lipids **2** and **3** to act as lung surfactants is reported.

Identification of a novel non-carbohydrate molecule that binds to the ribosomal A-site RNA

pp 5987–5990

Shawn P. Maddaford,* Mina Motamed, Kevin B. Turner,
Min Soo K. Choi, Jailall Ramnauth,
Suman Rakhit, Robert R. Hudgins,
Daniele Fabris and Philip E. Johnson*

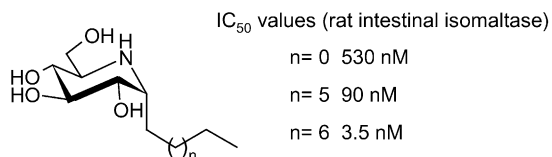


We report the identification of a novel compound that binds to the *Escherichia coli* ribosomal A-site. We observed binding using NMR, mass spectrometry, and docking techniques and demonstrate that the compound binds in the same position as occupied by aminoglycoside antibiotics.

 α -1-C-Alkyl-1-deoxynojirimycin derivatives as potent and selective inhibitors of intestinal isomaltase: remarkable effect of the alkyl chain length on glycosidase inhibitory profile

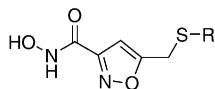
pp 5991–5995

Guillaume Godin, Philippe Compain,* Olivier R. Martin,* Kyoko Ikeda, Liang Yu and Naoki Asano

**Isoxazole-3-hydroxamic acid derivatives as peptide deformylase inhibitors and potential antibacterial agents**

pp 5997–6000

Patrizia Calì,* Lars Nærum, Seema Mukhija and Anders Hjelmencrantz

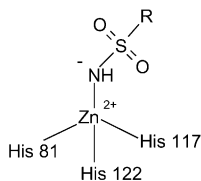


The synthesis and initial in vitro evaluation of isoxazole-3-hydroxamic acid derivatives as a new class of PDF inhibitors are reported.

Carbonic anhydrase inhibitors. Inhibition of the prokaryotic beta and gamma-class enzymes from *Archaea* with sulfonamides

pp 6001–6006

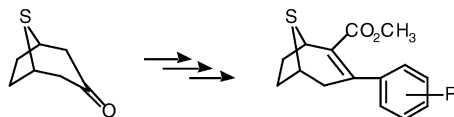
Sabrina Zimmerman, Alessio Innocenti, Angela Casini, James G. Ferry, Andrea Scozzafava and Claudiu T. Supuran*



Synthesis of 8-thiabicyclo[3.2.1]oct-2-enes and their binding affinity for the dopamine and serotonin transporters

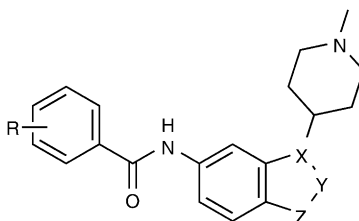
pp 6007–6010

Peter C. Meltzer,* Duy-Phong Pham-Huu and Bertha K. Madras


Design, synthesis and evaluation of bicyclic benzamides as novel 5-HT_{1F} receptor agonists

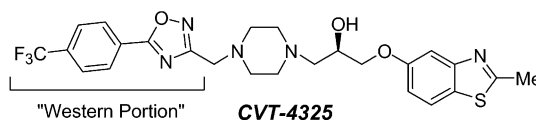
pp 6011–6016

Deyi Zhang,* Dan Kohlman, Joseph Krushinski, Sidney Liang, Bai-Ping Ying, John E. Reilly, Sean R. Dinn, David B. Wainscott, Suzanne Nutter, Wendy Gough, David L. G. Nelson, John M. Schaus and Yao-Chang Xu

The synthesis and evaluation of structurally novel 5-HT_{1F} receptor agonists are reported.
CVT-4325: a potent fatty acid oxidation inhibitor with favorable oral bioavailability

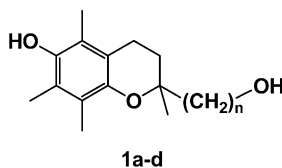
pp 6017–6021

Elfatih Elzein, Prabha Ibrahim, Dmitry O. Koltun, Ken Rehder, Kevin D. Shenk, Timothy A. Marquart, Bob Jiang, Xiaofen Li, Reina Natero, Yuan Li, Marie Nguyen, Suresh Kerwar, Nancy Chu, Daniel Soohoo, Jia Hao, Victoria Y. Maydanik, David A. Lustig, Dewan Zeng, Kwan Leung and Jeff A. Zablocki*

New inhibitors of palmitoyl-CoA oxidation are based on the introduction of nitrogen heterocycles in the 'Western Portion' of the molecule. SAR studies led to the discovery of CVT-4325, a potent FOXi (IC₅₀ = 380 nM, rat mitochondria) with favorable PK properties (*F* = 93%, *t*_{1/2} = 13.6 h, dog).
Tocopherol long chain fatty alcohols decrease the production of TNF- α and NO radicals by activated microglial cells

pp 6023–6026

Thierry Muller, Luc Grandbarbe, Eleonora Morga, Paul Heuschling and Bang Luu*

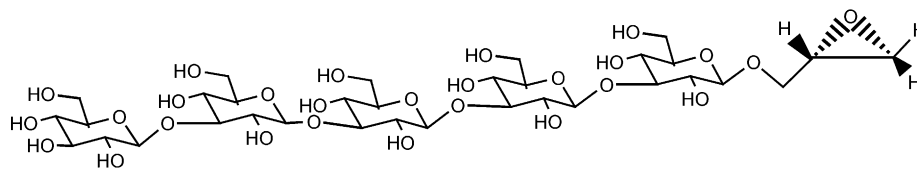


Tocopherol derivatives were found to strongly modulate microglial activation induced by lipopolysaccharide.

Synthesis, (1→3)- β -D-glucanase-binding ability and phytoalexin-elicitor activity of (*R*)-2,3-epoxypropyl (1→3)- β -D-pentaglucoide

pp 6027–6029

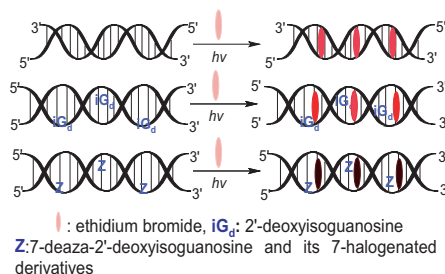
Gang-Liang Huang,* Xin-Ya Mei, Man-Xi Liu and Tian-Cai Liu



Fluorescence quenching of parallel-stranded DNA bound ethidium bromide: the effect of 7-deaza-2'-deoxyisoguanosine and 7-halogenated derivatives

pp 6031–6034

Hong Li, Xiaohua Peng and Frank Seela*



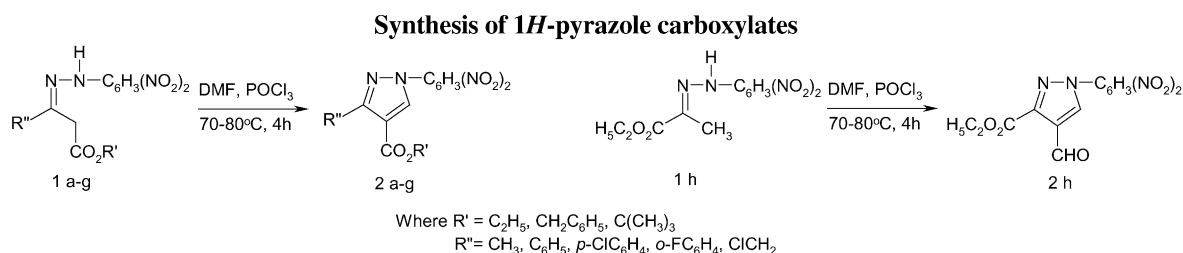
The fluorescence quenching of ethidium bromide in base-modified parallel-stranded DNA was studied.



Design, synthesis and anti-microbial activity of 1*H*-pyrazole carboxylates

pp 6035–6040

Radhakrishnan Sridhar, Paramasivam T. Perumal,* Sundaresan Etti, Guruswamy Shanmugam, Mondikalipudur N. Ponnuswamy, Vaiyapuri R. Prabavathy and Narayanasamy Mathivanan

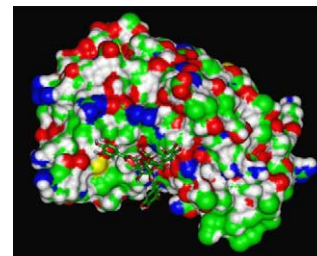


Antiviral compounds from traditional Chinese medicines *Galla Chinese* as inhibitors of HCV NS3 protease

pp 6041–6044

Deliang Duan, Zhengquan Li, Hongpeng Luo, Wei Zhang, Lirong Chen and Xiaojie Xu*

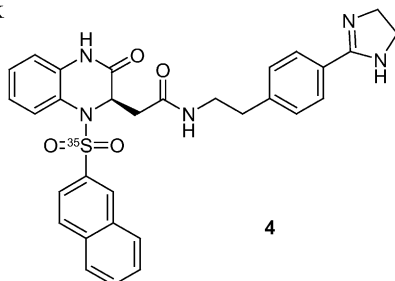
Under the guidance of bioassay, we purified 1,2,6-tri-*O*-galloyl- β -D-glucose, 1,2,3,6-tetra-*O*-galloyl- β -D-glucose, and 1,2,3,4,6-penta-*O*-galloyl- β -D-glucose from *Galla Chinese*, inhibited HCV NS3 protease with IC_{50} of 1.89, 0.75, and 1.60 μ M, respectively.



Development of an efficient and selective radioligand for bradykinin B₁ receptor occupancy studies

pp 6045–6048

Dai-Shi Su,* M. Kristine Markowitz, Kathy L. Murphy, Bang-Lin Wan, Matthew M. Zrada, C. Meacham Harrell, Stacy S. O'Malley, J. Fred Hess, Rick W. Ransom, Ray S. Chang, Michael A. Wallace, Conrad E. Raab, Dennis C. Dean, Douglas J. Pettibone, Roger M. Freidinger and Mark G. Bock

**3-(2-Methoxytetrahydrofuran-2-yl)pyrazoles: a novel class of potent, selective cyclooxygenase-2 (COX-2) inhibitors**

pp 6049–6052

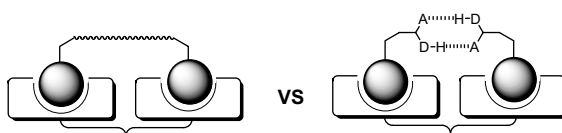
Ramani R. Ranatunge,* Richard A. Earl, David S. Garvey, David R. Janero, L. Gordon Letts, Allison M. Martino, Madhavi G. Murty, Stewart K. Richardson, David J. Schwalb, Delano V. Young and Irina S. Zemtseva

The synthesis of a series of novel 3-(2-methoxytetrahydrofuran-2-yl)pyrazoles and their in vitro cyclooxygenase-2 (COX-2) inhibitory activity in human whole blood (HWB) are reported.

Design of bivalent ligands using hydrogen bond linkers: synthesis and evaluation of inhibitors for human β -tryptase

pp 6053–6056

Roy J. Vaz, Zhongli Gao, James Pribish, Xin Chen, Julian Levell, Larry Davis, Eva Albert, Maurice Brollo, Antonio Ugolini, Dona M. Cramer, Jennifer Cairns, Keith Sides, Feng Liu, Jennifer Kwong, Jiesheng Kang, Sam Rebello, Michael Elliot, HengKeang Lim, Vinolia Chellaraj, Robert W. Singleton and Yi Li*

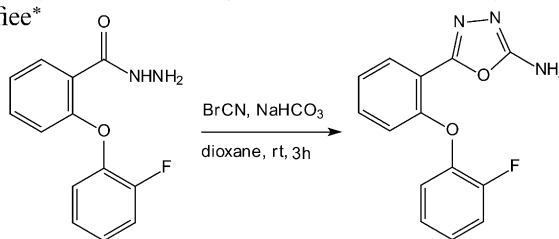


Alternative to a covalent linker, hydrogen bonds can be used to link ligands for maintaining simultaneous interactions with multiple binding sites. This is exemplified by the synthesis and evaluation of amide derivatives as potent inhibitors of human β -tryptase.

Synthesis and anticonvulsant activity of new 2-substituted-5-[2-(2-fluorophenoxy)phenyl]-1,3,4-oxadiazoles and 1,2,4-triazoles

pp 6057–6059

Ali Almasirad, Sayyed A. Tabatabai, Mehrdad Faizi, Abbas Kebriaeezadeh, Nazila Mehrabi, Afshin Dalvandi and Abbas Shafiee*



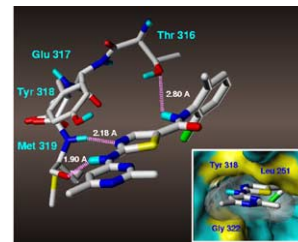
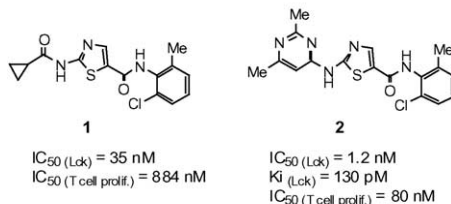
1,3,4-Oxadiazole and 1,2,4-triazole derivatives were prepared as anticonvulsant agents. Pharmacological evaluation was performed on the synthesized compounds.

Discovery of novel 2-(aminoheteroaryl)-thiazole-5-carboxamides as potent and orally active Src-family kinase $p56^{Lck}$ inhibitors

pp 6061–6066

Ping Chen,* Derek Norris, Jagabandhu Das, Steven H. Spergel, John Wityak, Leslie Leith, Rulin Zhao, Bang-Chi Chen, Sidney Pitt, Suhong Pang, Ding Ren Shen, Rosemary Zhang, Henry F. De Fex, Arthur M. Doweiko, Kim W. McIntyre, David J. Shuster, Kamelia Behnia, Gary L. Schieven and Joel C. Barrish

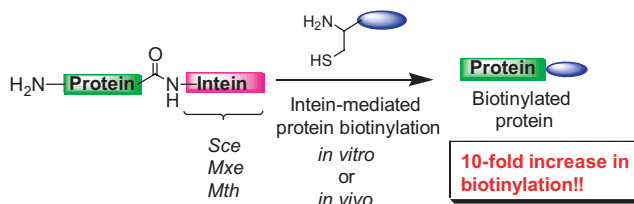
A series of substituted 2-(aminoheteroaryl)-thiazole-5-carboxamide analogs have been synthesized as novel, potent inhibitors of the Src-family kinase $p56^{Lck}$. Among them, compound **2** displayed superior in vitro potency and excellent in vivo efficacy.



Improving the intein-mediated, site-specific protein biotinylation strategies both in vitro and in vivo

pp 6067–6070

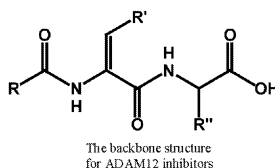
Lay-Pheng Tan, Rina Y. P. Lue, Grace Y. J. Chen and Shao Q. Yao*



Structure-based virtual screening and biological evaluation of potent and selective ADAM12 inhibitors

pp 6071–6074

Myungsok Oh, Isak Im, Yong Jae Lee, Young Hoon Kim, Jeong Hyeok Yoon, Hye Gyeong Park, Shigeki Higashiyama, Yong-Chul Kim* and Woo Jin Park*

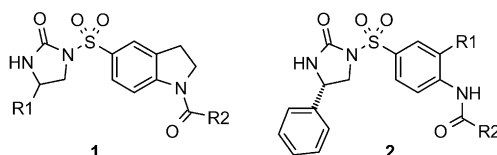


The virtual screening for the potent and selective ADAM12 inhibitors ($IC_{50} \leq 50 \text{ nm}$) is reported.

Novel diarylsulfonylurea derivatives as potent antimitotic agents

pp 6075–6078

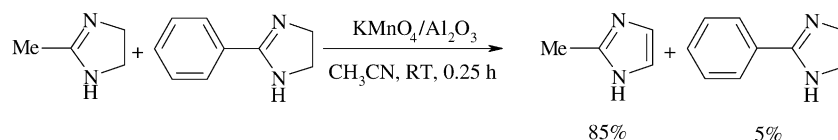
Semi Kim,* Ji Hyun Park, Sun-Young Koo, Jung In Kim, Min-Hyeung Kim, Ji Eun Kim, Kiwon Jo, Hwan Geun Choi, Sung Bae Lee and Sang-Hun Jung



Novel diarylsulfonylurea derivatives have been synthesized and identified as potent inhibitors of tubulin polymerization and cancer cell proliferation. Furthermore, these compounds were also efficacious against multidrug-resistant cancer cells.

Alumina supported potassium permanganate: an efficient reagent for chemoselective dehydrogenation of 2-imidazolines under mild conditions pp 6079–6082

Mohammad Abdollahi-Alibeik, Iraj Mohammadpoor-Baltork* and Mohammad Ali Zolfigol

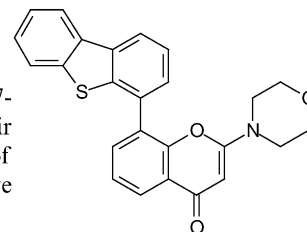


An efficient method for the oxidation of 2-imidazolines to their corresponding imidazoles using $\text{KMnO}_4/\text{Al}_2\text{O}_3$ under very mild reaction conditions is reported. Selective oxidation of 2-alkylimidazolines was also performed in the presence of 2-arylimidazolines and other functional groups such as sulfide, ether, aldehyde, acetal and THP ether.

Identification of a highly potent and selective DNA-dependent protein kinase (DNA-PK) inhibitor (NU7441) by screening of chromenone libraries pp 6083–6087

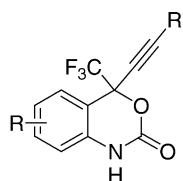
Justin J. J. Leahy, Bernard T. Golding, Roger J. Griffin,* Ian R. Hardcastle, Caroline Richardson, Laurent Rigoreau and Graeme C. M. Smith

A solution-phase multiple-parallel synthesis approach was employed for the preparation of 6-, 7- and 8-aryl-substituted chromenone libraries, which were screened as inhibitors of the DNA repair enzyme DNA-dependent protein kinase (DNA-PK). These studies resulted in the identification of 8-dibenzothiophen-4-yl-2-morpholin-4-yl-chromen-4-one (NU7441) as a highly potent and selective DNA-PK inhibitor ($\text{IC}_{50} = 14 \text{ nM}$), exhibiting ATP-competitive inhibition kinetics.



QSAR modelling of HIV-1 reverse transcriptase inhibition by benzoxazinones using a combination of P_VSA and pharmacophore feature descriptors pp 6089–6094

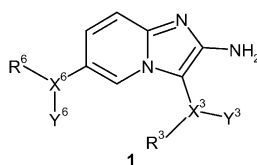
S. Balaji, C. Karthikeyan, N. S. Hari Narayana Moorthy and Piyush Trivedi*



A novel series of HIV-1 reverse transcriptase inhibitors was subjected to quantitative structure–activity relationship analysis (QSAR) employing a novel set of P_VSA descriptors.

Aminoimidazo[1,2-a]pyridines as a new structural class of cyclin-dependent kinase inhibitors. Part 1: Design, synthesis, and biological evaluation pp 6095–6099

Carlos Jaramillo,* J. Eugenio de Diego, Chafiq Hamdouchi, Elizabeth Collins, Heather Keyser, Concha Sánchez-Martínez, Miriam del Prado, Bryan Norman, Harold B. Brooks, Scott A. Watkins, Charles D. Spencer, Jack Alan Dempsey, Bryan D. Anderson, Robert M. Campbell, Tellie Leggett, Bharvin Patel, Richard M. Schultz, Juan Espinosa, Michal Vieth, Faming Zhang and David E. Timm



Synthesis of 2-aminoimidazo[1,2-a]pyridines **1** and their evaluation as CDK2 inhibitors is described.

A comparative binding study of modified Bovine Immunodeficiency Virus TAR RNA against its Tat peptide

pp 6101–6105

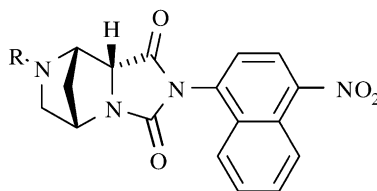
Jeffrey B.-H. Tok,* Lanrong Bi and Shuying Huang

The synthesis and binding studies of a series of both wt and mutant bovine immunodeficiency virus (BIV) TAR RNA constructs against its Tat peptide are reported. Understanding the requirements that enable RNA construct binding properties, especially at its hairpin loop or internal bulge, would afford potential therapeutic approaches to control the BIV life cycle.

The synthesis and evaluation of [2.2.1]-bicycloazahydantoin s as androgen receptor antagonists

pp 6107–6111

Aaron Balog,* Mark E. Salvati, Weifang Shan, Arvind Mathur, Leslie W. Leith, Donna D. Wei, Ricardo M. Attar, Jieping Geng, Cheryl A. Rizzo, Chihuei Wang, Stanley R. Krystek, John S. Tokarski, John T. Hunt, Marco Gottardis and Roberto Weinmann

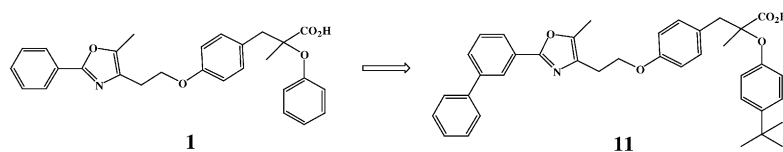


A novel series of [2.2.1]-bicycloazahydantoin s has been designed and synthesized in an enantiospecific manner. Several of these compounds were found to act as antagonists to the androgen receptor.

Conversion of human-selective PPAR α agonists to human/mouse dual agonists: a molecular modeling analysis

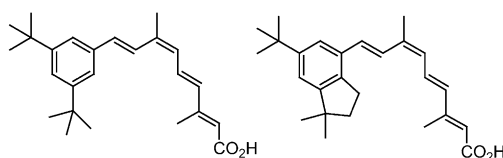
pp 6113–6116

Minmin Wang,* Leonard L. Winneroski,* Robert J. Ardecky, Robert E. Babine, Dawn A. Brooks, Garret J. Etgen, Darrell R. Hutchison, Raymond F. Kauffman, Aaron Kunkel, Dale E. Mais, Chahrzad Montrose-Rafizadeh, Kathleen M. Ogilvie, Brian A. Oldham, Mary K. Peters, Christopher J. Rito, Deepa K. Rungta, Allie E. Tripp, Sarah B. Wilson, Yanping Xu, Richard W. Zink and James R. McCarthy*

**9-*cis*-Retinoic acid analogues with bulky hydrophobic rings: new RXR-selective agonists**

pp 6117–6122

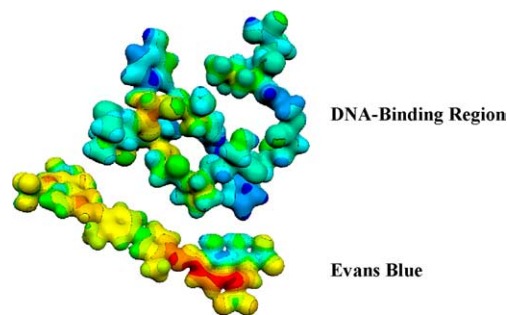
Rosana Alvarez, M. Jesús Vega, Sabrina Kammerer, Aurélie Rossin, Pierre Germain, Hinrich Gronemeyer and Angel R. de Lera*



Evans Blue is an inhibitor of nuclear factor-kappa B (NF- κ B)-DNA binding**pp 6123–6127**

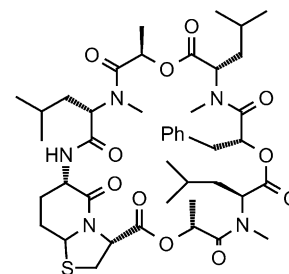
Rakesh K. Sharma, Masami Otsuka, Vineet Pande, Jun-ichiro Inoue and Maria João Ramos*

Evans Blue is reported as an inhibitor of NF- κ B-DNA binding, at a low concentration of 100 μ M. Molecular modeling studies suggest a possible binding mode consistent with the experimental results.

**Chimeric cyclodepsipeptides as mimetics for the anthelmintic PF1022A****pp 6129–6132**

Hubert Dyker, Achim Harder and Jürgen Scherckenbeck*

In the anthelmintic cyclooctadepsipeptide PF1022A didepsipeptide units have been exchanged for the β -turn mimetics (D)-Pro-(L)-Pro and BTD in order to elucidate the functional role of the depsipeptide backbone. Analogues have been identified, which show an improved anthelmintical activity compared to the natural product. Preliminary structure–activity relationships suggest a symmetrical conformation to be the biological active one.

**OTHER CONTENTS**

Corrigendum

Contributors to this issue

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*Corresponding author

①* Supplementary data available via ScienceDirect

COVER

The cover graphic shows the schematic representation both of the nitric oxide (NO \cdot) pathway in vascular homeostasis and of the oxidative hypothesis of atherosclerosis. Antioxidant/NO-donor hybrids could display protective roles against atherosclerosis [Cena, C.; Boschi, D.; Tron, G. C.; Chegaev, K.; Lazzarato, L.; Di Stillo, A.; Aragno, M.; Fruttero, R.; Gasco, A. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5971–5974]. This graphic has been adapted from a figure by T. Eberhardt and J. Loscalzo in *Nitric Oxide and the Cardiovascular System*; Loscalzo, J., Vita, J. A., Eds.; Humana Press: Totowa, 2000; p 275.

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