

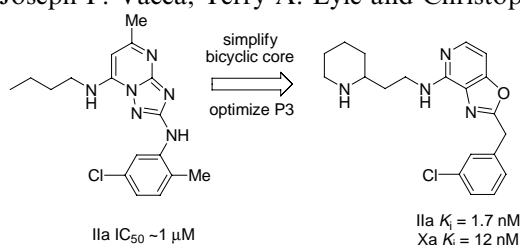
Contents

ARTICLES

Development of an oxazolopyridine series of dual thrombin/factor Xa inhibitors via structure-guided lead optimization

pp 4411–4416

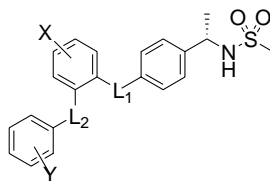
James Z. Deng, Daniel R. McMasters, Philippe M. A. Rabbat, Peter D. Williams, Craig A. Coburn, Youwei Yan, Lawrence C. Kuo, S. Dale Lewis, Bobby J. Lucas, Julie A. Krueger, Berta Strulovici, Joseph P. Vacca, Terry A. Lyle and Christopher S. Burgey*



Triaryl bis-sulfones as cannabinoid-2 receptor ligands: SAR studies

pp 4417–4420

Bandarpalle B. Shankar,* Brian J. Lavey,* Guowei Zhou, James A. Spitler, Ling Tong, Razia Rizvi, De-Yi Yang, Ronald Wolin, Joseph A. Kozlowski, Neng-Yang Shih, Jie Wu, R. William Hipkin, Waldemar Gonsiorek and Charles A. Lunn



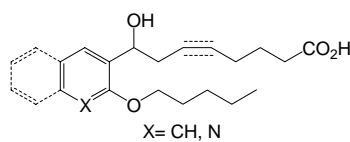
SAR studies on recently reported triaryl bis-sulfone cannabinoid CB2 receptor ligands are described. Modification of aryl substitution and their respective linkers gives compounds that are highly potent and selective for CB2. One compound is shown to be an orally available CB2-selective inverse agonist.



Synthesis of new carbo- and heterocyclic analogues of 8-HETE and evaluation of their activity towards the PPARs

pp 4421–4426

Frédéric Caijo, Paul Mosset,* René Grée,* Valérie Audinot-Bouchez, Jean Boutin, Pierre Renard, Daniel-Henri Caignard and Catherine Dacquet

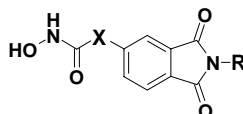


A new class of dual PPARs α and γ agonists has been developed. Most of these derivatives have a good activity but the quinoline-derived products appear as the most promising compounds.

Design and synthesis of phthalimide-type histone deacetylase inhibitors

pp 4427–4431

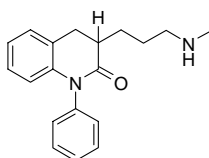
Chihiro Shinji, Takanori Nakamura, Satoko Maeda, Minoru Yoshida, Yuichi Hashimoto and Hiroyuki Miyachi*



The design, synthesis, and HDAC-inhibitory activity of hydroxamic acids with a substituted phthalimide group are reported.

1-Aryl-3,4-dihydro-1H-quinolin-2-one derivatives, novel and selective norepinephrine reuptake inhibitors pp 4432–4437

Christopher D. Beadle, John Boot, Nicholas P. Camp,* Nancy Dezutter, Jeremy Findlay, Lorna Hayhurst, John J. Masters, Roberta Penariol and Magnus W. Walter



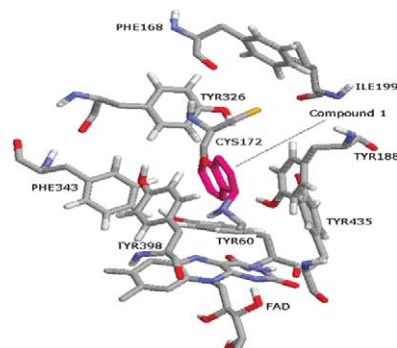
A novel series of 1-aryl-3,4-dihydro-1H-quinolin-2-ones has been discovered as potent and selective norepinephrine reuptake inhibitors. Efficient synthetic routes have been developed, which allow for the multi-gram preparation of both final targets and advanced intermediates for SAR expansion.

Docking studies on monoamine oxidase-B inhibitors: Estimation of inhibition constants (K_i) of a series of experimentally tested compounds

pp 4438–4446

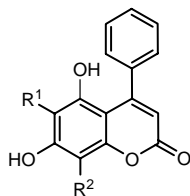
Mustafa Toprakçı and Kemal Yelekçi*

A series of experimentally tested (1–10) model compounds has been docked computationally to the active site of the MAO-B enzyme. The AutoDock 3.0.5 program was employed to perform automated molecular docking. The free energies of binding (ΔG) and inhibition constants (K_i) of the docked compounds were calculated by the Lamarckian Genetic Algorithm (LGA) of AutoDock 3.0.5. Typical docking result: compound 1 (Rasagiline) in the active site of MAO-B.

**4-Phenylcoumarins as HIV transcription inhibitors**

pp 4447–4450

Luis M. Bedoya, Manuela Beltrán, Rocío Sancho, Dionisio A. Olmedo, Sonsoles Sánchez-Palomino, Esther del Olmo, José L. López-Pérez,* Eduardo Muñoz, Arturo San Feliciano and José Alcamí*

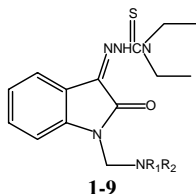


The inhibitory activity of natural 4-phenylcoumarins on HIV replication, NF- κ B and Tat is evaluated.

Synthesis and evaluation of anti-HIV activity of isatin β -thiosemicarbazone derivatives

pp 4451–4455

Tanushree Ratan Bal, Balasubramani Anand, Perumal Yogeewari and Dharmarajan Sriram*

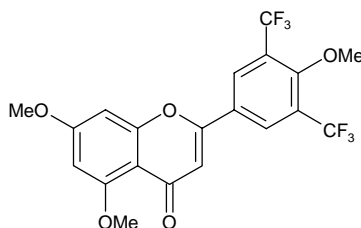


A series of isatin β -thiosemicarbazones derivatives was synthesized and evaluated for anti-HIV activity in HTLV-III_B strain in CEM cell line. Compound **6** was found to be the most active compound with an EC₅₀ value of 2.62 μ M.

Trifluoromethylation of flavonoids and anti-tumor activity of the trifluoromethylated flavonoid derivatives

pp 4456–4458

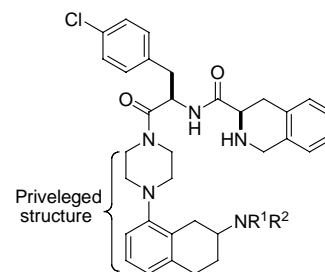
Cai-Ling Wang, Hong-Qi Li, Wei-Dong Meng and Feng-Ling Qing*

**Privileged structure-based ligands for melanocortin receptors—tetrahydroquinolines, indoles, and aminotetralines**

pp 4459–4462

Matthew J. Fisher,* Ryan T. Backer, Saba Husain, Hansen M. Hsiung, Jeffrey T. Mullaney, Thomas P. O'Brian, Paul L. Ornstein, Roger R. Rothhaar, John M. Zgombick and Karin Briner

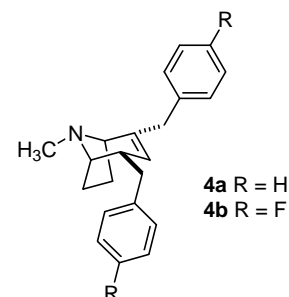
Tetrahydroquinolines, indoles, and aminotetralines provide useful privileged structures for the construction of ligands with affinity for melanocortin 4 receptors.

**Synthesis and evaluation of a series of tropane analogues as novel vesicular monoamine transporter-2 ligands**

pp 4463–4466

Guangrong Zheng, Linda P. Dwoskin, Agripina G. Deaciuc and Peter A. Crooks*

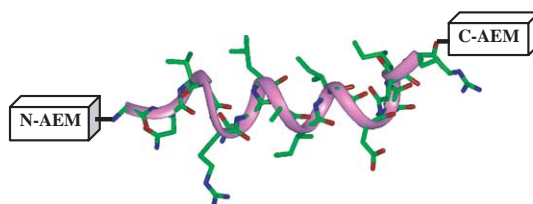
A series of tropane derivatives has been synthesized as lobelane analogues and evaluated for their binding affinity at the vesicular monoamine transporter-2 (VMAT2), and at α 4 β 2* and α 7* nicotinic acetylcholine receptors. The trop-2-ene analogues **4a** and **4b** exhibited good affinity and high selectivity for VMAT2.



A chemical strategy to promote helical peptide–protein interactions involved in apoptosis

pp 4467–4469

Dongxiang Liu, Bin Yang, Rong Cao and Ziwei Huang*



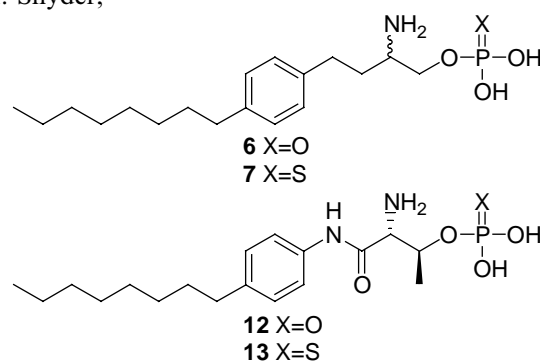
A new strategy for studying and mimicking helical peptide–protein interactions involved in apoptosis.

Synthesis, stability, and implications of phosphothioate agonists of sphingosine-1-phosphate receptors

pp 4470–4474

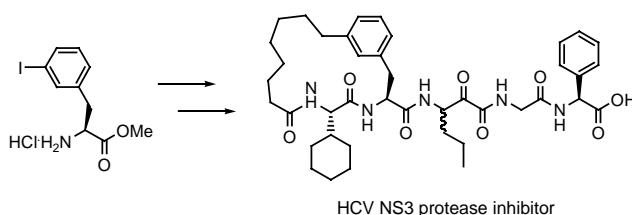
Frank W. Foss, Jr., Jeremy J. Clemens, Michael D. Davis, Ashley H. Snyder, Molly A. Zigler, Kevin R. Lynch and Timothy L. Macdonald*

The synthesis and biological activity of phosphothioates, as subtype selective sphingosine-1-phosphate receptor agonists, are described. Sphingosine-1-phosphate receptor agonist **12** is degraded to its alcohol in vivo. Compared to their phosphate precursors, phosphothioate compounds **7** and **13** were shown to induce lymphopenia for protracted intervals in vivo.

**Synthesis and biological activity of macrocyclic inhibitors of hepatitis C virus (HCV) NS3 protease**

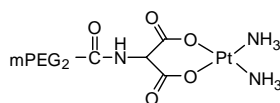
pp 4475–4478

Kevin X. Chen,* F. George Njoroge, Andrew Prongay, John Pichardo, Vincent Madison and Viyyoor Girijavallabhan

**Synthesis and cytotoxic activity of platinum complex immobilized by branched polyethylene glycol**

pp 4479–4483

Yong Ren, Haitao Zhang and Junlian Huang*



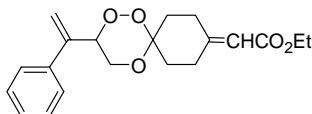
Two-arm branched mPEG was synthesized and used as carrier for immobilization of CDDP.



New orally active spiro 1,2,4-trioxanes with high antimalarial potency

pp 4484–4487

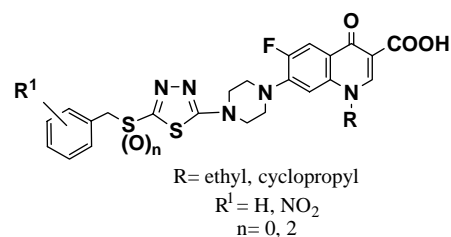
Chandan Singh,* Heetika Malik and Sunil K. Puri

**Synthesis and antibacterial activity of *N*-(5-benzylthio-1,3,4-thiadiazol-2-yl) and *N*-(5-benzylsulfonyl-1,3,4-thiadiazol-2-yl)piperazinyl quinolone derivatives**

pp 4488–4492

Alireza Foroumadi,* Saeed Emami, Abdolreza Hassanzadeh, Majid Rajaei, Kazem Sokhanvar, Mohammad Hassan Moshafi and Abbas Shafiee

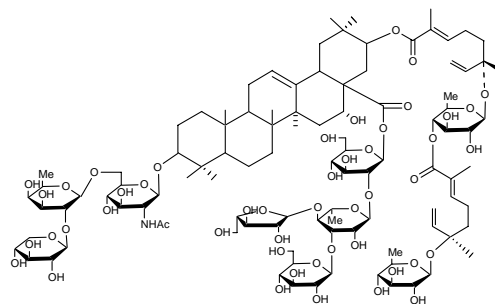
A series of *N*-(5-benzylthio-1,3,4-thiadiazol-2-yl) and *N*-(5-benzylsulfonyl-1,3,4-thiadiazol-2-yl) derivatives of piperazinyl quinolones was synthesized and evaluated for antibacterial activity. Some of these derivatives exhibit comparable or more potent activity against Gram-positive bacteria; *Staphylococcus aureus* and *Staphylococcus epidermidis*, with respect to the reference drugs. The SAR of this series indicates that both the structure of the benzyl unit and the S or SO₂ linker dramatically impact antibacterial activity.

**An antitumor compound julibroside J₂₈ from *Albizia julibrissin***

pp 4493–4495

Hong Liang, Wen-yong Tong, Yu-ying Zhao,* Jing-rong Cui and Guang-zhong Tu

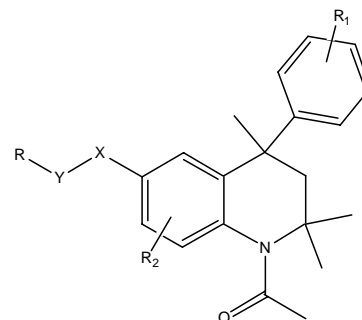
The structure of a new triterpenoid saponin julibroside J₂₈, isolated from *Albizia julibrissin*, has been determined on the basis of comprehensive spectroscopic analysis. Julibroside J₂₈ had marked antitumor activity.

**First QSAR report on FSH receptor antagonistic activity: Quantitative investigations on physico-chemical and structural features among 6-amino-4-phenyltetrahydroquinoline derivatives**

pp 4496–4501

E. Manivannan and S. Prasanna*

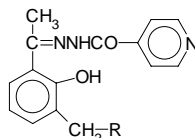
QSAR analysis on recently reported 6-amino-4-phenyltetrahydroquinoline derivatives as FSH receptor antagonists has been presented.



Synthesis and in vitro and in vivo antimycobacterial activity of isonicotinoyl hydrazones

pp 4502–4505

Dharmarajan Sriram,* Perumal Yogeewari and Kasinathan Madhu

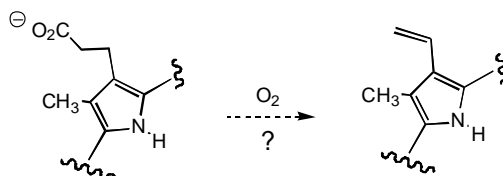
**1-15**

2-Hydroxy acetophenone react with isoniazid to form acid hydrazones. The C-Mannich bases of the above acid hydrazone were prepared by reacting them with formaldehyde and various secondary amines. Compound *N'*-{1-[2-hydroxy-3-(piperazin-1-ylmethyl)phenyl]ethylidene}isonicotinohydrazide **8** was found to be the most active compound with MIC of 0.56 $\mu\text{M/mL}$ and was more potent than isoniazide (MIC of 2.04 $\mu\text{M/mL}$).

The enigma of coproporphyrinogen oxidase: How does this unusual enzyme carry out oxidative decarboxylations to afford vinyl groups?

pp 4506–4509

Timothy D. Lash*



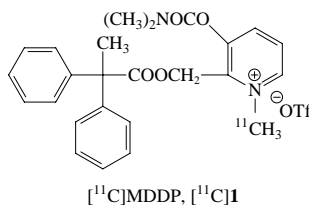
A new mechanism is proposed to explain how coproporphyrinogen oxidase performs two oxidative decarboxylations on a porphyrinogen substrate without the aid of cofactors or metal ions in the presence of molecular oxygen.

Facile synthesis and PET imaging of a novel potential heart acetylcholinesterase tracer

pp 4510–4514

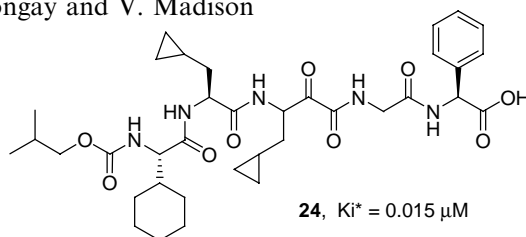
N-[^{11}C]methyl-3-[(dimethylamino)carbonyloxy]-2-(2',2'-diphenylpropionoxymethyl)pyridinium

Ji-Quan Wang, Michael A. Miller, Bruce H. Mock, John C. Lopshire, William J. Groh, Douglas P. Zipes, Gary D. Hutchins and Qi-Huang Zheng*

**[^{11}C]MDDP, [^{11}C]1****Hepatitis C virus NS3-4A serine protease inhibitors: Use of a P₂-P₁ cyclopropyl alanine combination for improved potency**

pp 4515–4519

S. Bogen,* A. K. Saksena, A. Arasappan, H. Gu, F. G. Njoroge, V. Girijavallabhan, J. Pichardo, N. Butkiewicz, A. Prongay and V. Madison

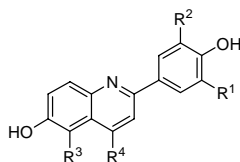
**24**, $K_i^* = 0.015 \mu\text{M}$

Modification of the P₂ and P₁ side chains of earlier P₃-capped α -ketoamide inhibitor of HCV NS3 serine protease **1** resulted in the discovery of compound **24** with about 10-fold improvement in potency.

ER β ligands. Part 4: Synthesis and structure–activity relationships of a series of 2-phenylquinoline derivatives

pp 4520–4525

An T. Vu,* Stephen T. Cohn, Eric S. Manas, Heather A. Harris and Richard E. Mewshaw

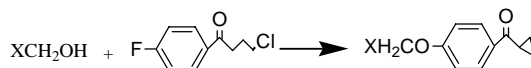


A series of 2-phenylquinoline derivatives was prepared and displayed high affinity and significant selectivity for estrogen receptor β .

An efficient synthesis of aryloxyphenyl cyclopropyl methanones: a new class of anti-mycobacterial agents

pp 4526–4530

Namrata Dwivedi, Neetu Tewari, V. K. Tiwari, Vinita Chaturvedi, Y. K. Manju, A. Srivastava, A. Giakwad, S. Sinha and R. P. Tripathi*

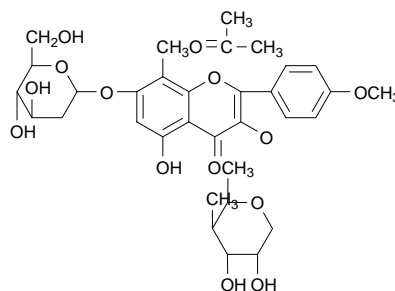


Aryloxy phenyl cyclopropyl methanones were synthesized and evaluated as new potent anti-tubercular agents.

Screening of active compounds as neuromedin U2 receptor agonist from natural products

pp 4531–4535

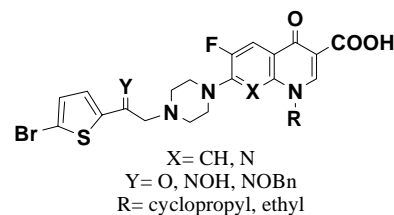
Xuxu Zheng,* Yinghe Hu, Jianhui Liu and Keqing Ouyang

**Synthesis and antibacterial activity of *N*-[2-(5-bromothiophen-2-yl)-2-oxoethyl] and *N*-[(2-5-bromothiophen-2-yl)-2-oximinoethyl] derivatives of piperazinyl quinolones**

pp 4536–4539

Alireza Foroumadi, Saeed Emami, Massood Mehni, Mohammad Hassan Moshafi and Abbas Shafiee*

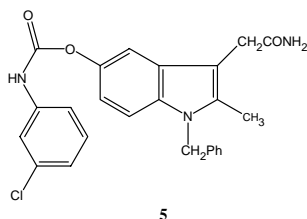
A series of *N*-[2-(5-bromothiophen-2-yl)-2-oxoethyl] and *N*-[2-(5-bromothiophen-2-yl)-2-oximinoethyl] derivatives of piperazinyl quinolones were synthesized and evaluated for antimicrobial activity. Some of these derivatives exhibit comparable or better activity against Gram-positive bacteria, than ciprofloxacin, norfloxacin and enoxacin as reference drugs.



Indole-5-phenylcarbamate derivatives as human non-pancreatic secretory phospholipase A2 inhibitor

pp 4540–4542

Ying Liu,* Xiao-feng Han, Chang-kang Huang, Xin Hao and Lu-Hua Lai*



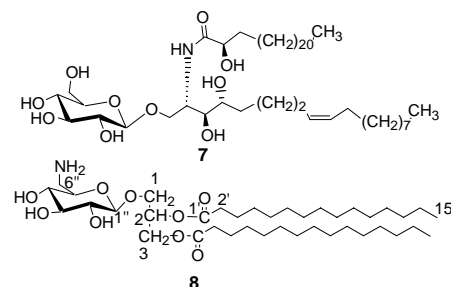
The synthesis of the human non-pancreatic secretory phospholipase A2 inhibitor ($IC_{50} = 1.81 \pm 0.59 \mu M$) is reported.

Glycolipids and other constituents from *Desmodium gangeticum* with antileishmanial and immunomodulatory activities

pp 4543–4546

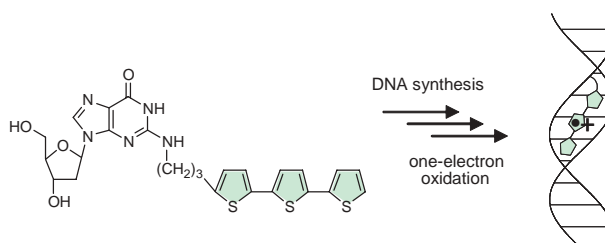
Pushpesh Kumar Mishra, Nasib Singh, Ghufuran Ahmad, Anuradha Dube and Rakesh Maurya*

Two glycolipids were identified from *Desmodium gangeticum* to possess antileishmanial and immunomodulatory activities. Aminoglucosyl-glycerolipid (**8**) was found to be novel.

**Synthesis and properties of terthiophene-modified oligodeoxynucleotides**

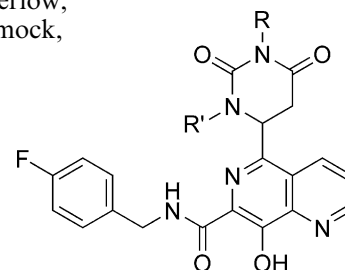
pp 4547–4549

Kiyohiko Kawai,* Akira Sugimoto, Hiroko Yoshida, Sachiko Tojo, Mamoru Fujitsuka and Tetsuro Majima*

**A series of 5-(5,6)-dihydrouracil substituted 8-hydroxy-[1,6]naphthyridine-7-carboxylic acid 4-fluorobenzylamide inhibitors of HIV-1 integrase and viral replication in cells**

pp 4550–4554

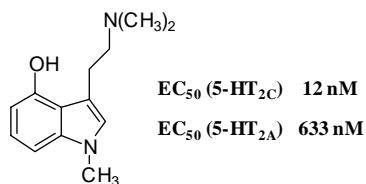
Mark W. Embrey,* John S. Wai, Timothy W. Funk, Carl F. Homnick, Debbie S. Perlow, Steven D. Young, Joseph P. Vacca, Daria J. Hazuda, Peter J. Felock, Kara A. Stillmock, Marc V. Witmer, Gregory Moyer, William A. Schleif, Lori J. Gabryelski, Lixia Jin, I-Wu Chen, Joan D. Ellis, Bradley K. Wong, Jiunn H. Lin, Yvonne M. Leonard, Nancy N. Tsou and Linghang Zhuang



SAR of psilocybin analogs: Discovery of a selective 5-HT_{2C} agonist

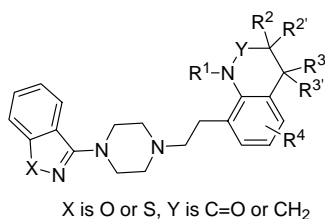
pp 4555–4559

Howard Sard,* Govindaraj Kumaran, Cynthia Morency, Bryan L. Roth, Beth Ann Toth, Ping He and Louis Shuster

**8-Substituted 3,4-dihydroquinolinones as a novel scaffold for atypical antipsychotic activity**

pp 4560–4563

Jamie M. Singer,* Bridget M. Barr, Linda L. Coughenour, Tracy F. Gregory and Michael A. Walters

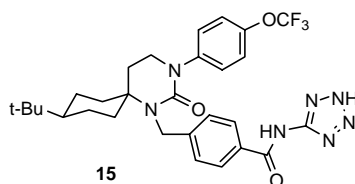


The synthesis and biological activity of novel 8-substituted 3,4-dihydroquinolinones, tetrahydroquinolines, and *N*-acyltetrahydroquinolines are disclosed.

Discovery of novel, potent, and orally active spiro-urea human glucagon receptor antagonists

pp 4564–4569

Dong-Ming Shen,* Fengqi Zhang, Edward J. Brady, Mari Rios Candelore, Qing Dallas-Yang, Victor D.-H. Ding, Jasminka Dragovic, William P. Feeney, Guoqiang Jiang, Peggy E. McCann, Steve Mock, Sajjad A. Qureshi, Richard Saperstein, Xiaolan Shen, Constantin Tamvakopoulos, Xinchun Tong, Laurie M. Tota, Michael J. Wright, Xiaodong Yang, Song Zheng, Kevin T. Chapman, Bei B. Zhang, James R. Tata and Emma R. Parmee



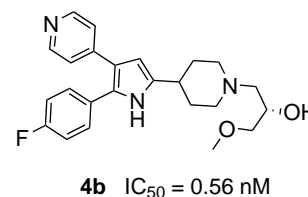
The discovery and SAR study of a novel spiro-urea series of human glucagon receptor antagonists such as **15** are presented.

Hydroxylated *N*-alkyl-4-piperidiny-2,3-diarylpyrrole derivatives as potent broad-spectrum anticoccidial agents

pp 4570–4573

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

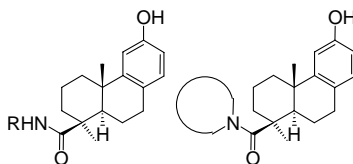
Diaryl-(4-piperidiny)-pyrrole derivatives bearing hydroxylated *N*-alkyl substituents have been synthesized and evaluated as anticoccidial agents.



Design, synthesis, and structure–activity relationship of podocarpic acid amides as liver X receptor agonists for potential treatment of atherosclerosis

pp 4574–4578

Weiguo Liu,* Steve Chen, James Dropinski, Lawrence Colwell, Michael Robins, Michael Szymonifka, Nancy Hayes, Neelam Sharma, Karen MacNaul, Melba Hernandez, Charlotte Burton, Carl P. Sparrow, John G. Menke and Sheo B. Singh*

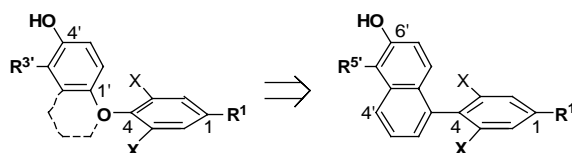


Discovery and development of podocarpic acid amides as LXR ligands are described.

A new class of high affinity thyromimetics containing a phenyl-naphthylene core

pp 4579–4584

Jon J. Hangeland,* Todd J. Friends, Arthur M. Doweyko, Karin Mellström, Johnny Sandberg, Marlena Grynfarb and Denis E. Ryono

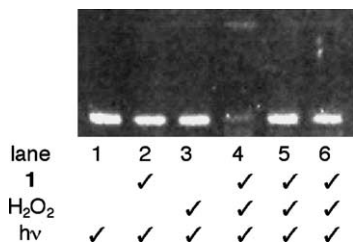


Examples of this new class of thyromimetics have sub-nanomolar binding affinities for TR, with an SAR that diverges from TR ligands containing a biaryl ether core.

The hydrogen peroxide induced enhancement of DNA cleavage in the ambient light photolysis of CpFe(CO)₂Ph: A potential strategy for targeting cancer cells

pp 4585–4588

Debra L. Mohler* and Thomas A. Shell

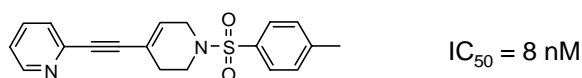


DNA cleavage by the ambient light photolysis of CpFe(CO)₂Ph (1) is increased by the presence of hydrogen peroxide, a species whose concentration is elevated in some cancer cells.


Cyclohexenyl- and dehydropiperidiny-alkynyl pyridines as potent metabotropic glutamate subtype 5 (mGlu5) receptor antagonists

pp 4589–4593

Peter C. Chua,* Johnny Y. Nagasawa, Leo S. Bleicher, Benito Munoz, Edwin J. Schweiger, Lida Tehrani, Jeffrey J. Anderson, Merryl Cramer, Janice Chung, Mitchell D. Green, Chris D. King, Grace Reyes-Manalo and Nicholas D. P. Cosford

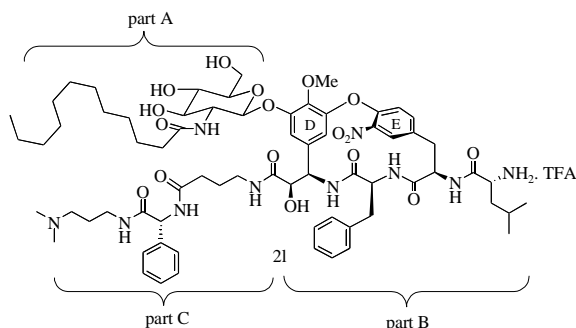


Identification of synthetic compounds active against VRE: the role of the lipidated aminoglucose and the structure of glycopeptide binding pocket

pp 4594–4599

Yanxing Jia, Eduardo Gonzalez-Zamora, Nianchun Ma, Zuosheng Liu, Michèle Bois-Choussy, Adriano Malabarba, Cristina Brunati and Jieping Zhu*

Synthesis of modified vancomycin binding pocket (D–O–E ring) incorporating a (*R*)- or (*S*)-configured secondary alcohol function at the AA4 position is described. The presence of both the lipidated aminoglucose (part A) and the structure of the 16-membered macrocycle (part B) are important for the observed activities of the modified vancomycin D–O–E ring against VRE. The polyamine appendage at the C-terminal (part C), on the other hand, improved the activity against vancomycin-sensitive strains.

**The synthesis and antioxidant activity of the Schiff bases of chitosan and carboxymethyl chitosan**

pp 4600–4603

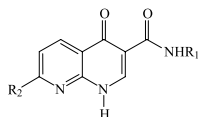
Zhanyong Guo, Rong Xing, Song Liu, Huahua Yu, Pibo Wang, Cuiping Li and Pengcheng Li*

The Schiff bases of chitosan and carboxymethyl chitosan (CMCTS) were synthesized and their antioxidant activity was assessed using an established system. The Schiff bases of chitosan and CMCTS have different scavenging ability on superoxide and hydroxyl radicals, which could be related to contents of the active hydroxyl and amino groups.

1,8-Naphthyridin-4-one derivatives as new ligands of A_{2A} adenosine receptors

pp 4604–4610

Clementina Manera,* Laura Betti, Tiziana Cavallini, Gino Giannaccini, Adriano Martinelli, Gabriella Ortore, Giuseppe Saccomanni, Letizia Trincavelli, Tiziano Tuccinardi and Pier Luigi Ferrarini

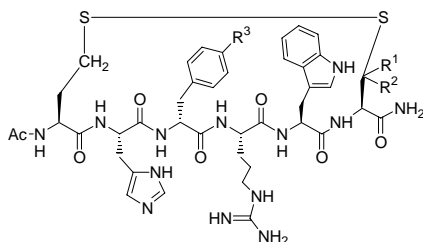


A series of 1,8-naphthyridine derivatives bearing various substituents in positions 3, 4, and 7 of the heterocyclic nucleus have been synthesized and evaluated for their affinity at the bovine and human adenosine receptors. The new compounds were found to lack the affinity towards A₁AR, whereas many of them are able to acquire an interesting affinity and selectivity for the A_{2A}AR.

Potent and selective MC-4 receptor agonists based on a novel disulfide scaffold

pp 4611–4614

Liang Z. Yan,* David Flora, Patrick Edwards, David L. Smiley, Paul J. Emmerson, Hansen M. Hsiung, Robert Gadski, JeAnne Hertel, Mark L. Heiman, Saba Husain, Thomas P. O'Brien, Steven D. Kahl, Lianshan Zhang, Richard D. DiMarchi and John P. Mayer*



MC-4R binding potency (K_i)

12 (R¹ = R² = R³ = H, K_i = 0.27 nM)

14 (R¹ = R² = H, R³ = F, K_i = 0.28 nM)

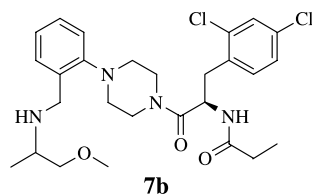
16 (R¹ = R² = CH₃, R³ = Cl, K_i = 0.05 nM)



Optimization of piperazinebenzylamines with a *N*-(1-methoxy-2-propyl) side chain as potent and selective antagonists of the human melanocortin-4 receptor

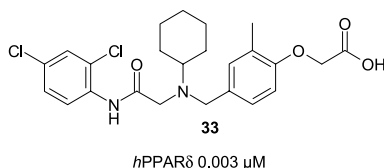
pp 4615–4618

Joseph Pontillo, Dragan Marinkovic, Joe A. Tran, Melissa Arellano, Beth A. Fleck, Jenny Wen, Fabio C. Tucci, Jodie Nelson, John Saunders, Alan C. Foster and Chen Chen*


Minor structural modifications convert a selective PPAR α agonist into a potent, highly selective PPAR δ agonist

pp 4619–4623

Stefan Weigand,* Hilmar Bischoff, Elke Dittrich-Wengenroth, Heike Heckroth, Dieter Lang, Andrea Vaupel and Michael Woltering

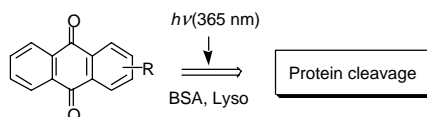


We report the solid-phase synthesis and pharmacological evaluation of a new series of small-molecule agonists of the human peroxisome proliferator-activated receptor δ (PPAR δ) based on a lead structure from our PPAR α program. Compound **33** showed good pharmacokinetics.

Anthraquinone derivatives as a new family of protein photocleavers

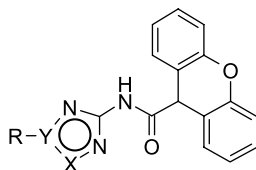
pp 4624–4627

Akane Suzuki, Masashi Hasegawa, Maiko Ishii, Shuichi Matsumura and Kazunobu Toshima*


9*H*-Xanthene-9-carboxylic acid [1,2,4]oxadiazol-3-yl- and (2*H*-tetrazol-5-yl)-amides as potent, orally available mGlu1 receptor enhancers

pp 4628–4631

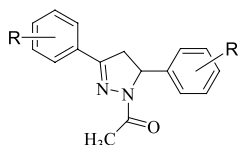
Eric Vieira,* Jörg Huwyler, Synèse Jolidon, Frédéric Knöflach, Vincent Mutel and Jürgen Wichmann



Small molecule mGluR1 enhancers **3** (X = O, Y = C) and **4** (X = Y = N) were synthesized as pharmacological tools for the study of the physiological roles mediated by mGlu1 receptors.

Synthesis of some pyrazole derivatives and preliminary investigation of their affinity binding to P-glycoprotein**pp 4632–4635**

Fedele Manna, Franco Chimenti, Rossella Fioravanti,* Adriana Bolasco, Daniela Secci, Paola Chimenti, Cristiano Ferlini and Giovanni Scambia



A series of substituted pyrazoline were synthesized and evaluated for their anticancer activity and for their ability to inhibit P-glycoprotein-mediated multidrug resistance.

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*Corresponding author

Ⓜ⁺ 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.

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

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ISSN 0960-894X