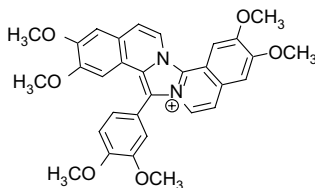


Contents

COMMUNICATIONS

Aggregation and G-quadruplex DNA-binding study of 6a,12a-diazadibenzo-[a,g]fluorenylium derivative pp 3627–3630

Bernard Juskowiak,* Elzbieta Galezowska, Natalia Koczorowska and Tadeusz W. Hermann

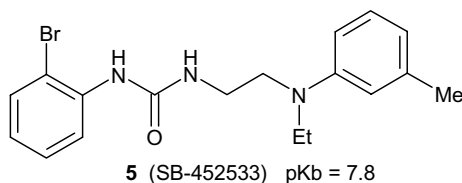


A new G-quadruplex selective ligand, fluorenylium derivative, binds preferentially with four-stranded DNA, it can bind weakly to the duplex and very weakly to ssDNA.

Discovery of small molecule antagonists of TRPV1

pp 3631–3634

Harshad K. Rami,* Mervyn Thompson, Paul Wyman, Jeffrey C. Jerman, Julie Egerton, Stephen Brough, Alexander J. Stevens, Andrew D. Randall, Darren Smart, Martin J. Gunthorpe and John B. Davis

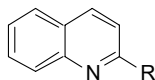


TRPV1 antagonist activity of **5** and the potential binding site of its quaternary salt is reported.

Biological evaluation of substituted quinolines

pp 3635–3638

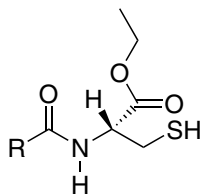
Xavier Franck, Alain Fournet, Eric Prina, Renaud Mahieux, Reynald Hocquemiller and Bruno Figadère*



Several 2-substituted quinolines were synthesized and evaluated against several protozoa and against HTLV-1 transformed cells.

Synthesis and pharmacological evaluation of amide conjugates of NSAIDs with L-cysteine ethyl ester, combining potent antiinflammatory and antioxidant properties with significantly reduced gastrointestinal toxicity pp 3639–3643

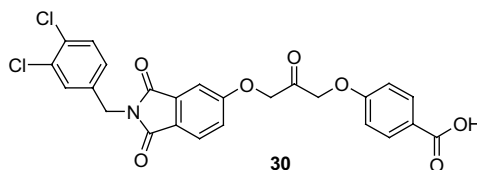
Dimitrios Galanakis,* Angeliki P. Kourounakis, Karyophyllis C. Tsiakitzis, Christos Doulgeris, Eleni A. Rekka, Antonios Gavalas, Constantina Kravaritou, Christos Charitos and Panos N. Kourounakis



R-COOH: common NSAIDs

Synthesis and evaluation of substrate-mimicking cytosolic phospholipase A₂ inhibitors—reducing the lipophilicity of the arachidonyl chain isostere pp 3645–3649

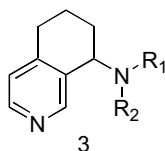
Iain Walters,* Colin Bennion, Stephen Connolly, Pamela J. Croshaw, Kim Hardy, Paul Hartopp, Clive G. Jackson, Sarah J. King, Louise Lawrence, Antonio Mete, David Murray, David H. Robinson, Linda Stein, Edward Wells and W. John Withnall



The high lipophilicity of a series of cytosolic phospholipase A₂ inhibitors has been reduced by the modification of a decyloxyphenyl chain designed to mimic the arachidonyl group of the natural substrate.

(±)8-Amino-5,6,7,8-tetrahydroisoquinolines as novel antinociceptive agents pp 3651–3654

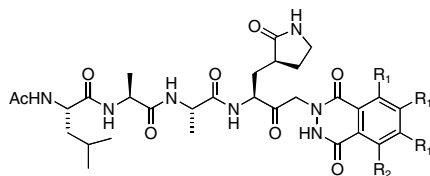
Małgorzata Dukat, Mohamed Taroua, Abdelaziz Dahdouh, Umamaheswar Siripurapu, M. Imad Damaj, Billy R. Martin and Richard A. Glennon*



Several tetrahydroisoquinolines **3** were evaluated as novel nACh ligands. Although lacking significant affinity at nACh receptors, some (in particular **3** where R₁ = Me, R₂ = Et) displayed potent antinociceptive actions in a tail-flick assay.

Structural variations in keto-glutamines for improved inhibition against hepatitis A virus 3C proteinase pp 3655–3658

Rajendra P. Jain and John C. Vederas*



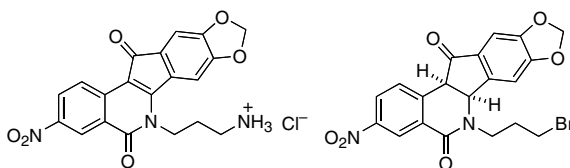
R₁ = H, F; R₂ = H, F, NO₂; IC₅₀ = 1.6–2.5 μM

A series of keto-glutamine tetrapeptide analogs containing a 2-oxo-pyrrolidine ring as a glutamine side chain mimic were synthesized, which show improved inhibition against hepatitis A virus 3C proteinase.

Synthesis of nitrated indenoisoquinolines as topoisomerase I inhibitors

pp 3659–3663

Andrew Morrell, Smitha Antony, Glenda Kohlhausen, Yves Pommier and Mark Cushman*

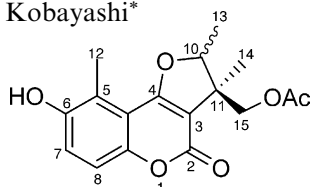


Substitution of the indenoisoquinoline system with an electron-withdrawing nitro group has been investigated as a strategy for increasing cytotoxicity and topoisomerase I inhibitory activity.

Antimitotic activity of glaupalol-related coumarins from *Glaucidium palmatum*

pp 3665–3668

Hiroshi Morita, Tomoka Dota and Jun'ichi Kobayashi*



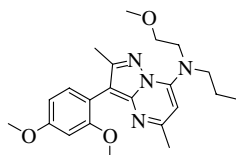
1: 10*S*11*R*
2: 10*R*11*R*

Two new coumarins, glaumacidines A (**1**) and B (**2**), and the related coumarins (**3–7**) have been isolated from the rhizomes of *Glaucidium palmatum* (Glaucidiaceae). The absolute configurations of **1** and **2** and *trans*- and *cis*-glaupadiols (**3** and **4**, respectively) were elucidated by spectroscopic data, chemical derivatization, and exciton chirality method. Glaupalol (**5**) enhanced the polymerization of tubulin and affected synergistically with paclitaxel on inhibition of KB cell proliferation.

Optimization of 3-phenylpyrazolo[1,5-*a*]pyrimidines as potent corticotropin-releasing factor-1 antagonists with adequate lipophilicity and water solubility

pp 3669–3673

Chen Chen,* Keith M. Wilcoxon, Charles Q. Huang, James R. McCarthy, Takung Chen and Dimitri E. Grigoriadis



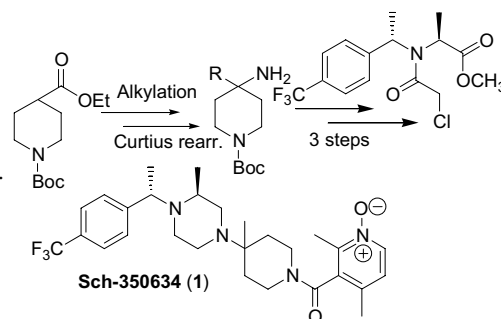
NBI 30545

Facile synthesis of 4-substituted-4-aminopiperidine derivatives, the key building block of piperazine-based CCR5 antagonists

pp 3675–3678

Xiao-Hua Jiang, Yan-Li Song and Ya-Qiu Long*

An efficient and convenient method for the synthesis of 4-differently substituted-4-aminopiperidine derivatives was described, employing isonipecotate as a starting material and Curtius rearrangement as a key step. With this key building block, we are able to efficiently synthesize piperazino-piperidine based CCR5 antagonist in a highly convergent manner free from toxic reagents such as diethylaluminum cyanide employed by previous procedures.



Novel δ^2 -isoxazolines as group II phospholipase A_2 inhibitors

pp 3679–3681

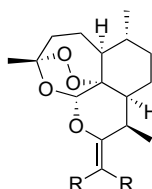
Basappa, M. Satish Kumar, S. Nanjunda Swamy, M. Mahendra, J. Shashidhara Prasad, B. S. Viswanath and K. S. Rangappa*

The synthesized imidazolyl substituted δ^2 -isoxazoline libraries were subjected to Phospholipase A_2 (PLA $_2$) enzyme inhibitory activity against snake venom source and their structure–activity relationship with respect to different groups attached to this moiety is reported for the first time. The crystal structure of the compound 2-butyl-5-chloro-3*H*-imidazolyl-4-carbaldehyde oxime **2**, an intermediate for the construction of δ^2 -isoxazoline libraries is reported. These compounds exerted a significant PLA $_2$ enzyme inhibitory activity against group II PLA $_2$. The in vivo activity on mice of selected compounds **3bI** and **3bIV** shows the comparable anti-inflammatory activity with the known standard ursolic acid.

Synthesis and antiangiogenic activity of *exo*-olefinated deoxoartemisinin derivatives

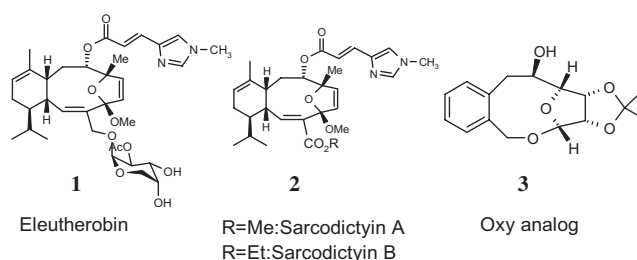
pp 3683–3686

Sangtae Oh, In Howa Jeong, Woon-Seob Shin* and Seokjoon Lee*

**Design, synthesis and cytotoxic studies on the simplified oxy analog of eleutherobin**

pp 3687–3689

S. Chandrasekhar,* V. Jagadeshwar, Ch. Narsihmulu, M. Sarangapani, D. R. Krishna, J. Vidyasagar, Dolly Vijay and G. Narahari Sastry*

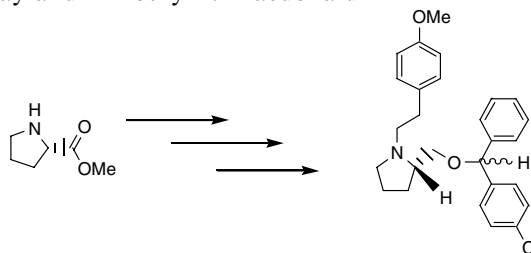


The oxy-B-ring of eleutherobin skeleton **3** retains the binding affinity to tubulin receptor.

Design, synthesis, and biological evaluation of novel T-Type calcium channel antagonists

pp 3691–3695

William F. McCalmont, Tiffany N. Heady, Jaclyn R. Patterson, Michael A. Lindenmuth, Doris M. Haverstick, Lloyd S. Gray and Timothy L. Macdonald

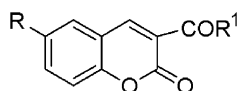


Several novel calcium influx inhibitors were synthesized, and biologically evaluated to gauge their relevance in cellular proliferation assays.

Inhibition of monoamine oxidases by coumarin-3-acyl derivatives: biological activity and computational study

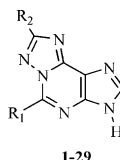
pp 3697–3703

Franco Chimenti, Daniela Secci,* Adriana Bolasco, Paola Chimenti, Arianna Granese, Olivia Befani, Paola Turini, Stefano Alcaro and Francesco Ortuso

**QSAR of adenosine receptor antagonists. Part 3: Exploring physicochemical requirements for selective binding of 1,2,4-triazolo[5,1-*i*]purine derivatives with human adenosine A₃ receptor subtype**

pp 3705–3709

Kunal Roy,* J. Thomas Leonard and Chandana Sengupta

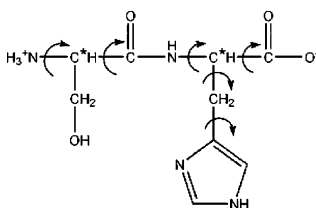


Considering potential of selective adenosine A₃ receptor antagonists in the development of prospective therapeutic agents, an attempt has been made to explore selectivity requirements of 1,2,4-triazolo[5,1-*i*]purine derivatives for binding with cloned human adenosine A₃ receptor subtype.

Molecular modeling on DNA cleavage activity of seryl-histidine and related dipeptide

pp 3711–3714

Ming Sun, Yuan Ma, Sanhao Ji, Huanai Liu and Yufen Zhao*

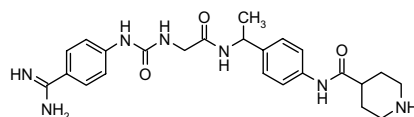


The key structural features for DNA cleaving activity were investigated.

Structure-based design of amidinophenylurea-derivatives for factor VIIa inhibition

pp 3715–3720

Otmar Klingler,* Hans Matter, Manfred Schudok, Monica Donghi, Joerg Czech, Martin Lorenz, Hans Peter Nestler, Hauke Szillat and Herman Schreuder

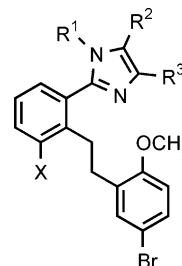


The amidinophenylurea scaffold was shown to provide an excellent template for the synthesis of novel and potent inhibitors of the blood coagulation factor VIIa. In this contribution we describe the structure-based design of potent ligands guided by X-ray crystallography, molecular modeling and docking studies. The design and synthetic efforts were directed towards novel modifications to explore the protease binding region close to the S4 subsite.

Synthesis and biological evaluation of imidazole-based small molecule antagonists of the melanocortin 4 receptor (MC4-R) pp 3721–3725

Thomas H. Marsilje,* Jonathan B. Roses, Emily F. Calderwood, Stephen G. Stroud, Nancy E. Forsyth, Christopher Blackburn, David L. Yowe, Wenyan Miao, Stacey V. Drabic, Marie D. Bohane, J. Scott Daniels, Ping Li, Lijun Wu, Michael A. Patane and Christopher F. Claiborne

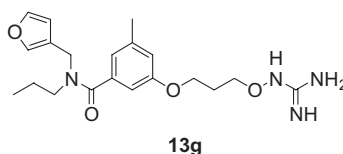
A novel series of imidazole-based small molecule antagonists of the melanocortin 4 receptor (MC4-R) is reported. Members of this series have been identified, which exhibit sub-micromolar binding affinity for the MC4-R, functional potency <100 nM, and good oral exposure in rat.



Oxyguanidines. Part 2: Discovery of a novel orally active thrombin inhibitor through structure-based drug design and parallel synthesis

pp 3727–3731

Tianbao Lu,* Thomas Markotan, Frank Coppo, Bruce Tomczuk, Carl Crysler, Stephen Eisennagel, John Spurlino, Lisa Gremminger, Richard M. Soll, Edward C. Giardino and Roger Bone

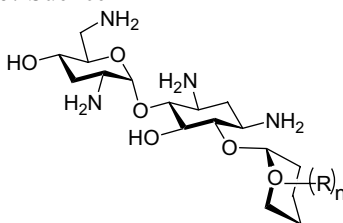


We report here a novel series of non-peptidic phenyl-based orally bioavailable thrombin inhibitors using oxyguanidines as guanidine bioisosteres through structure-based drug design and parallel synthesis.

Glyco-optimization of aminoglycosides: new aminoglycosides as novel anti-infective agents

pp 3733–3738

Sulan Yao,* Paulo W. M. Sgarbi, Kenneth A. Marby, David Rabuka, Sean M. O'Hare, Mayling L. Cheng, Mrunali Bairi, Changyong Hu, San-Bao Hwang, Chan-Kou Hwang, Yoshi Ichikawa, Pamela Sears and Steven J. Sucheck*

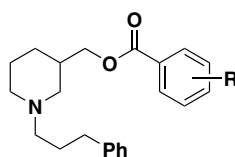


R = H, Me, OH, NH₂, NMe₂, etc.



Structure activity studies of ring E analogues of methyllycaconitine. Part 2: Synthesis of antagonists to the $\alpha 3\beta 4^*$ nicotinic acetylcholine receptors through modifications to the ester pp 3739–3742

Stephen C. Bergmeier,* Khadiga A. Ismail, Kristjan M. Arason, Susan McKay, Darrell L. Bryant and Dennis B. McKay

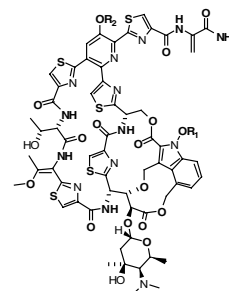


A series of ring E analogues of methyllycaconitine have been prepared and identified as potent functional antagonists at the $\alpha 3\beta 4^*$ nicotinic acetylcholine receptor.

Synthesis and antibacterial activity of O-substituted nocathiacin I derivatives

pp 3743–3746

B. Narasimhulu Naidu,* Margaret E. Sorenson, Thomas Hudyma,
Xiaofan Zheng, Yunhui Zhang, Joanne J. Bronson, Michael J. Pucci,
Junius M. Clark and Yasutsugu Ueda

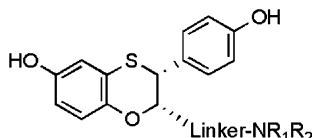


The synthesis and antibacterial activity of nocathiacin I analogues is described.

Estrogen receptor ligands. Part 5: The SAR of dihydrobenzoxathiins containing modified basic side chains

pp 3747–3751

Qiang Tan,* Elizabeth T. Birzin, Wanda Chan, Yi Tien Yang, Lee-Yuh Pai, Edward C. Hayes,
Carolyn A. DaSilva, Frank DiNinno, Susan P. Rohrer, James M. Schaeffer
and Milton L. Hammond

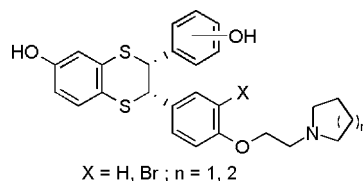


Modifications to the basic side chain region lead to a further understanding of the SAR of the dihydrobenzoxathiin class of SERAMs (Selective Estrogen Receptor Alpha Modulators).

Estrogen receptor ligands. Part 6: Synthesis and binding affinity of dihydrobenzodithiins

pp 3753–3755

Qiang Tan,* Elizabeth T. Birzin, Wanda Chan, Yi Tien Yang, Lee-Yuh Pai,
Edward C. Hayes, Carolyn A. DaSilva, Frank DiNinno, Susan P. Rohrer, James M. Schaeffer
and Milton L. Hammond

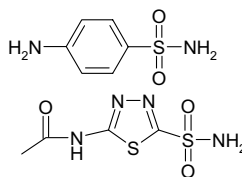


The synthesis and biological activity of dihydrobenzodithiins, as ER α -selective estrogen receptor ligands, are described.

Carbonic anhydrase inhibitors. Inhibition of cytosolic isozyme XIII with aromatic and heterocyclic sulfonamides: a novel target for the drug design

pp 3757–3762

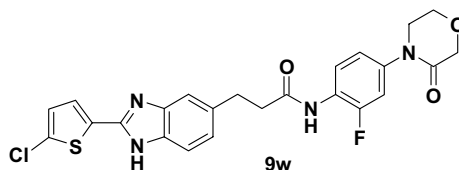
Jonna M. Lehtonen, Seppo Parkkila, Daniela Vullo, Angela Casini, Andrea Scozzafava
and Claudiu T. Supuran*



Halothiophene benzimidazoles as P1 surrogates of inhibitors of blood coagulation factor Xa

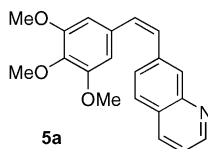
pp 3763–3769

Werner W. K. R. Mederski,* Dieter Dorsch, Soheila Anzali, Johannes Gleitz, Bertram Cezanne and Christos Tsaklakidis

**A new family of quinoline and quinoxaline analogues of combretastatins**

pp 3771–3774

Concepción Pérez-Melero, Ana B. S. Maya, Benedicto del Rey, Rafael Peláez, Esther Caballero and Manuel Medarde*

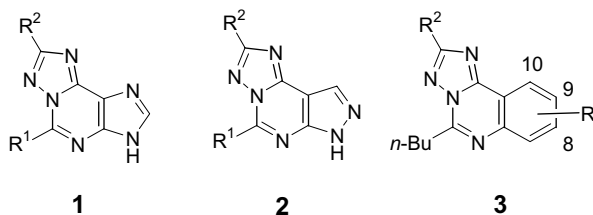


The synthesis and biological evaluation of quinoline and quinoxaline analogues of combretastatin A-4 are described.

Structure–activity relationships of adenosine A₃ receptor ligands: new potential therapy for the treatment of glaucoma

pp 3775–3779

Takashi Okamura,* Yasuhisa Kurogi, Kinji Hashimoto, Seiji Sato, Hiroshi Nishikawa, Kimio Kiryu and Yoshimitsu Nagao

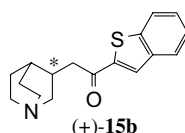


Structure–activity relationships (SAR) of fused 1,2,4-triazolo[1,5-*c*]pyrimidines (**1**, **2**, and **3**) were performed.

(+)-3-[2-(Benzo[*b*]thiophen-2-yl)-2-oxoethyl]-1-azabicyclo[2.2.2]octane as potent agonists for the α₇ nicotinic acetylcholine receptor

pp 3781–3784

Ryo Tatsumi,* Kohji Seio, Masakazu Fujio, Jiro Katayama, Takashi Horikawa, Kenji Hashimoto and Hiroshi Tanaka

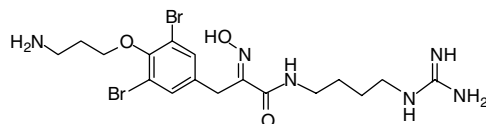


A series of 3-substituted 1-azabicyclo[2.2.2]octanes was discovered as the α₇ nicotinic acetylcholine receptor agonists.

Synthesis of a bromotyrosine-derived natural product inhibitor of mycothiol-S-conjugate amidase

pp 3785–3788

Brandon Fetterolf and Carole A. Bewley*

**Specific inhibition effects of *N*-pentafluorobenzyl-1-deoxynojirimycin on human CD4+ T cells**

pp 3789–3792

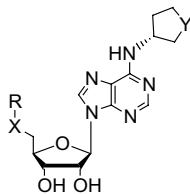
Xiao-Lian Zhang,* Min Liu, Peng Xie, Shuhui Wan, Jia Tao Ye, Xiang Zhou* and Jianguo Wu

We first synthesized *N*-pentafluorobenzyl-1-deoxynojirimycin (5F-DNM), one new derivative of 1-deoxynojirimycin (DNM). It was found that 5F-DNM remarkably inhibited the secretion of IL-4 from human PBMCs and had a specific inhibition on the expression of CD4 molecules. 5F-DNM, much less toxic than cyclosporin A, might be used as a new candidate of immunosuppressant for specifically treating Th2-mediated immune diseases.

Structure–affinity relationships of 5'-aromatic ethers and 5'-aromatic sulfides as partial A₁ adenosine agonists, potential supraventricular anti-arrhythmic agents

pp 3793–3797

Christopher F. Morrison,* Elfatih Elzein, Bob Jiang, Prabha N. Ibrahim, Timothy Marquart, Venkata Palle, Kevin D. Shenk, Vaibhav Varkhedkar, Tenning Maa, Lin Wu, Yuzhi Wu, Dewan Zeng, Irving Fong, David Lustig, Kwan Leung and Jeff A. Zablocki

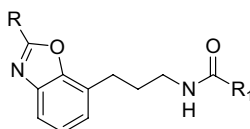


Potent partial A₁ AdoR agonists have been discovered.

**Synthesis and structure–activity relationship of novel benzoxazole derivatives as melatonin receptor agonists**

pp 3799–3802

Li-Qiang Sun,* Jie Chen, Marc Bruce, Jeffrey A. Deskus, James R. Epperson, Katherine Takaki, Graham Johnson, Lawrence Iben, Cathy D. Mahle, Elaine Ryan and Cen Xu

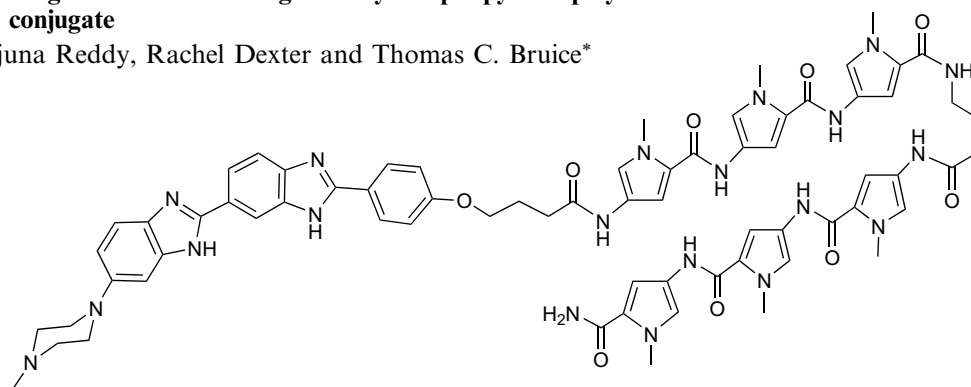


A series of benzoxazole derivatives was synthesized and evaluated as melatoninerbic ligands. The binding affinity of these compounds for human MT₁ and MT₂ receptors was determined using 2-[¹²⁵I]-iodomelatonin as the radioligand. From this series of benzoxazole derivatives, compounds **14** and **17** were identified as melatonin receptor agonists.

DNA sequence recognition in the minor groove by hairpin pyrrole polyamide–Hoechst 33258 analogue conjugate

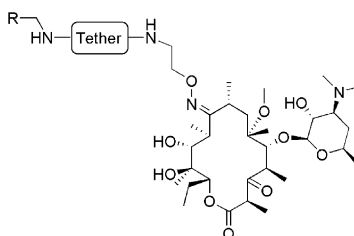
pp 3803–3807

Putta Mallikarjuna Reddy, Rachel Dexter and Thomas C. Bruice*


Synthesis and antibacterial activity of novel bifunctional macrolides

pp 3809–3813

Irin Akritopoulou-Zanze,* Kathleen M. Phelan, Thomas G. Marron, Hong Yong, Zhenkun Ma, Greg G. Stone, Melissa M. Daly, Dena M. Hensey, Angela M. Nilius and Stevan W. Djuric

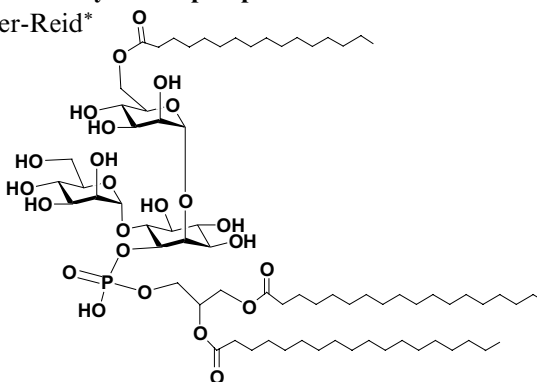


We report the discovery of a novel class of macrolide antibiotics that have improved antibacterial activity against Ery-resistant organisms.

Synthesis of a key *Mycobacterium tuberculosis* biosynthetic phosphoinositide intermediate

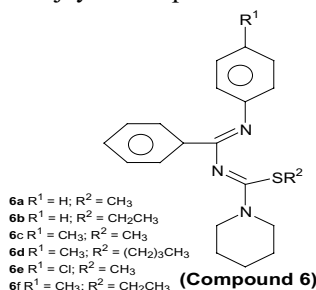
pp 3815–3819

K. N. Jayaprakash, Jun Lu and Bert Fraser-Reid*


Amidine derived 1,3-diazabuta-1,3-dienes as potential antibacterial and antifungal agents

pp 3821–3824

Preet M. S. Bedi,* Mohinder P. Mahajan and Vijay K. Kapoor

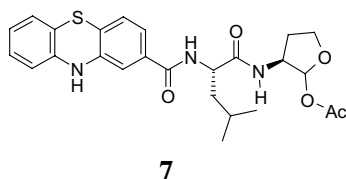


The synthesis and antimicrobial activity of amidine derived 1,3-diazabuta-1,3-diene derivatives are reported.

Novel dual inhibitors of calpain and lipid peroxidation

pp 3825–3828

Serge Auvin,* Bernadette Pignol, Edith Navet, Dominique Pons, Jean-G. Marin, Dennis Bigg and Pierre-E. Chabrier

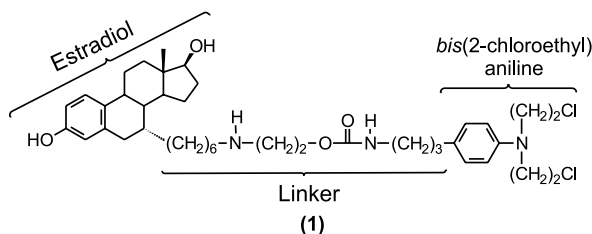


A series of hybrid compounds possessing calpain inhibitory and antioxidant properties has been synthesized. These compounds showed good inhibitory potencies in both activities. In addition, compound **7** provided effective protection against glial cell death induced by maitotoxin.

Design, synthesis, and evaluation of estradiol-linked genotoxicants as anti-cancer agents

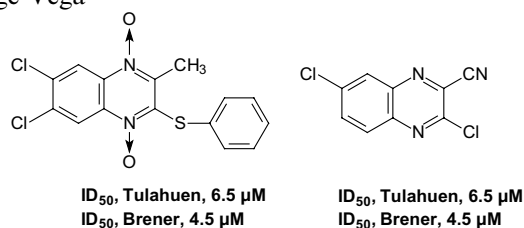
pp 3829–3833

U. Sharma, J. C. Marquis, A. Nicole Dinaut, S. M. Hillier, B. Fedeles, P. T. Rye, J. M. Essigmann* and R. G. Croy*

**Quinoxaline *N,N'*-dioxide derivatives and related compounds as growth inhibitors of *Trypanosoma cruzi*. Structure–activity relationships**

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Gabriela Aguirre, Hugo Cerecetto, Rossanna Di Maio, Mercedes González, María Elena Montoya Alfaro, Andrés Jaso, Belén Zarranz, Miguel Á. Ortega, Ignacio Aldana and Antonio Monge-Vega*

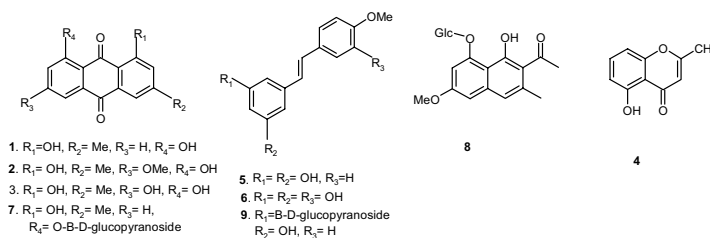


From our quinoxaline-library were identified new anti-chagasic leaders.

Yeast and mammalian α-glucosidase inhibitory constituents from Himalayan rhubarb *Rheum emodi* Wall.ex Meisson

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K. Suresh Babu, Ashok K. Tiwari, Pullela V. Srinivas, Amtul Z. Ali, B. China Raju and J. Madhusudana Rao*




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*Corresponding author

+ Supplementary data available via ScienceDirect

COVER

Cover figure provided by **Indraneel Ghosh**, Department of Chemistry, University of Arizona. The cover depicts the **Dual Surface Selection** methodology developed by the author: the blue helix of htBI (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htBI (center) allows for functional selection against thrombin (right) [Rajagopal, S.; Meza-Romero, R.; Ghosh, I. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1389].



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