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Bioorganic &
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Chemistry

Bioorganic & Medicinal Chemistry Vol. 13, No. 13, 2005

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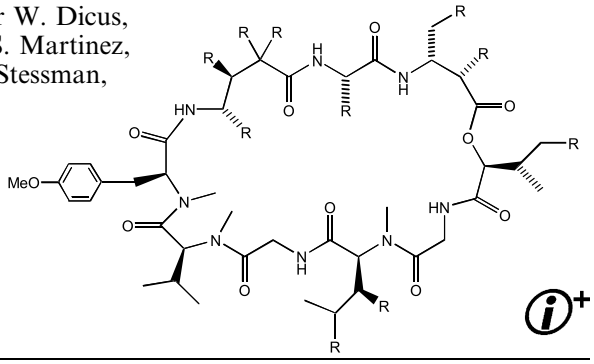
Dolastatin 11 conformations, analogues and pharmacophore pp 4138–4152

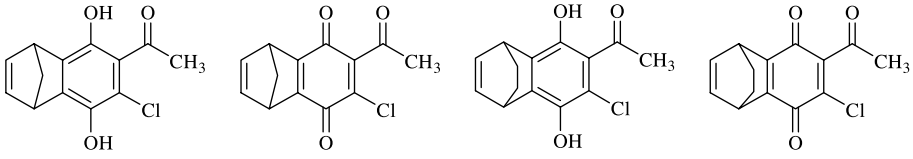
Md. Ahad Ali, Robert B. Bates,* Zackary D. Crane, Christopher W. Dicus, Michelle R. Gramme, Ernest Hamel, Jacob Marcischak, David S. Martinez, Kelly J. McClure, Pichaya Nakkiew, George R. Pettit, Chad C. Stessman, Bilal A. Sufi and Gayle V. Yarick

Syntheses and structure–activity relationships of 20 analogues where *R*s vary help define the pharmacophore.



Studies on quinones. Part 39: Synthesis and leishmanicidal activity of acylchloroquinones and hydroquinones pp 4153–4159

Jaime A. Valderrama,* Carlos Zamorano, M. Florencia González, Eric Prina and Alain Fournet

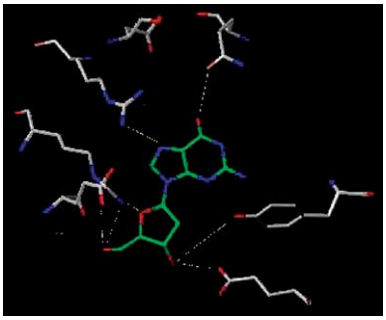


Novel 6-acetyl-7-chloro-1,4-alkanonaphthalenes have been synthesized from 2,5-dihydroxy-6-chloroacetophenone. The leishmanicidal activities of these compounds and their precursors were examined.

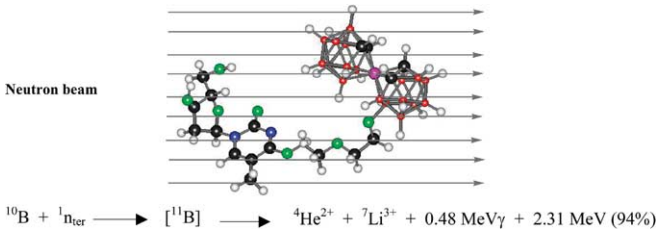
Docking simulation with a purine nucleoside specific homology model of deoxycytidine kinase, a target enzyme for anticancer and antiviral therapy pp 4160–4167

Jayaseharan Johnsamuel,* Staffan Eriksson, Marcos Oliveira and Werner Tjarks

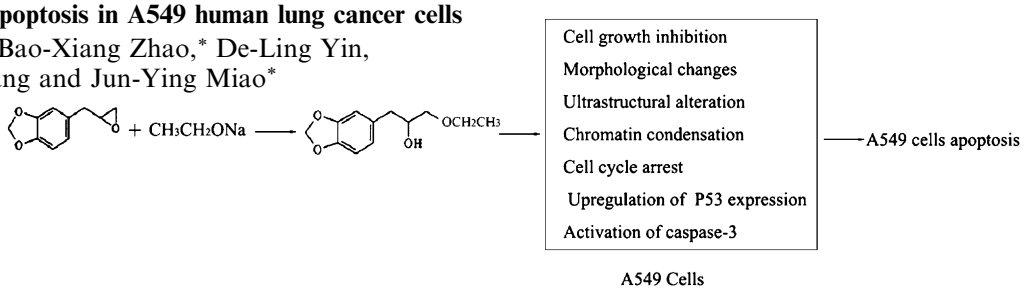
A homology model of deoxycytidine kinase specific for purine nucleoside was developed based on the crystal structure of purine nucleoside bound deoxyguanosine kinase as the template. Comparative docking simulations with this homology model were carried out using deoxycytidine, cytidine, cytarabine, cladribine, deoxyadenosine, and deoxyguanosine as substrates.



Towards new boron carriers for boron neutron capture therapy: metallacarboranes and their nucleoside conjugates **pp 4168–4175**
Zbigniew J. Leśnikowski,* Edyta Paradowska, Agnieszka B. Olejniczak, Mirosława Studzińska, Petra Seekamp, Uw Schüßler, Detlef Gabel, Raymond F. Schinazi and Jaromir Plešek

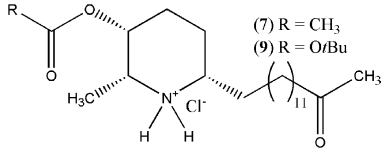


Discovery of a novel small molecule, 1-ethoxy-3-(3,4-methylenedioxyphenyl)-2-propanol, that induces apoptosis in A549 human lung cancer cells **pp 4176–4183**
Ai-Ying Du, Bao-Xiang Zhao,* De-Ling Yin, Shang-Li Zhang and Jun-Ying Miao*



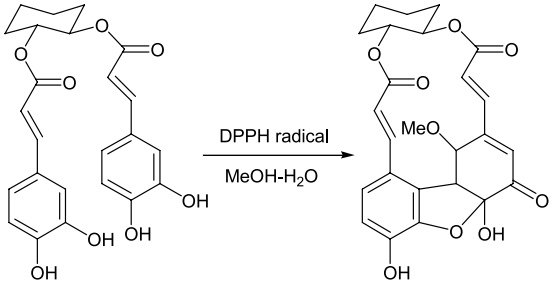
3,4-(Methylenedioxy)-1-(2′,3′-epoxypropyl)-benzene reacted with sodium ethoxide in alcohol to yield 1-ethoxy-3-(3,4-methylenedioxyphenyl)-2-propanol (EOD). EOD induced apoptosis in A549 human lung cancer cells by up-regulation of P53 protein, blocking cell cycle partly at G_1 phase and activation of caspase-3.

New selective acetylcholinesterase inhibitors designed from natural piperidine alkaloids **pp 4184–4190**
Cláudio Viegas, Jr., Vanderlan S. Bolzani, Luísa S. B. Pimentel, Newton G. Castro, Rafael F. Cabral, Rodrigo S. Costa, Corinne Floyd, Mônica S. Rocha, Maria C. M. Young, Eliezer J. Barreiro and Carlos A. M. Fraga*



The two new piperidine modified alkaloids **7** and **9** are described as selective acetylcholinesterase inhibitors, IC_{50} = 7.3 and 15.1 μM, respectively.

Radical scavenging activity of dicaffeoyloxycyclohexanes: Contribution of an intramolecular interaction of two caffeoyl residues **pp 4191–4199**
Shizuka Saito, Satoshi Kurakane, Miyuki Seki, Eiji Takai, Takanori Kasai and Jun Kawabata*



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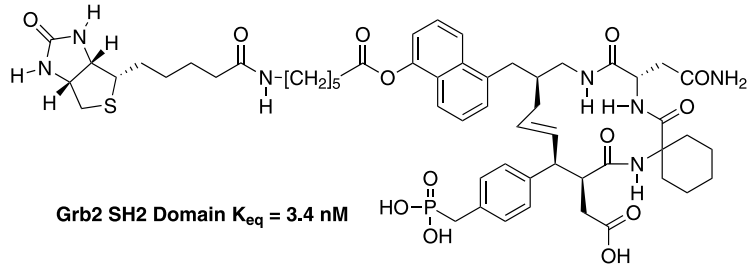

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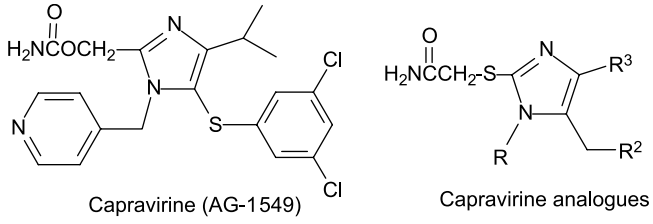
Yasser M. Loksha, Ahmed A. El-Barbary, Mahmoud A. El-Badawi, Claus Nielsen and Erik B. Pedersen*



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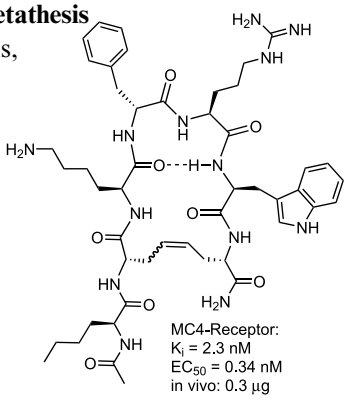

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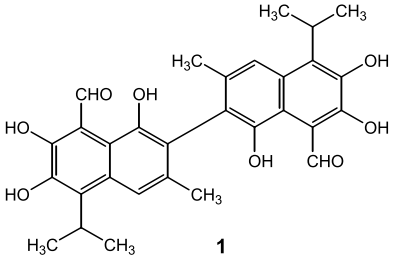
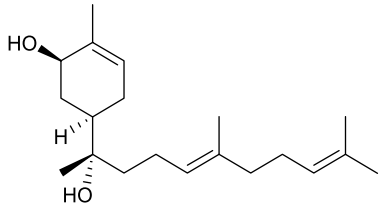


A prenylbisabolane with NF-κB inhibiting properties from Cascarilla (*Croton eluteria*) **pp 4238–4242**
Claudio Campagnuolo, Ernesto Fattorusso,* Francesca Petrucci, Orazio Taglialatela-Scafati, Giovanni Appendino, Nieves Marquez and Eduardo Muñoz



5-Arylidene-2-imino-4-thiazolidinones: Design and synthesis of novel anti-inflammatory agents **pp 4243–4252**
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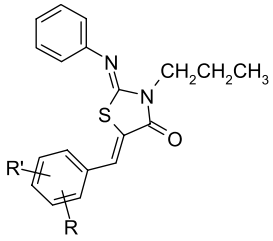
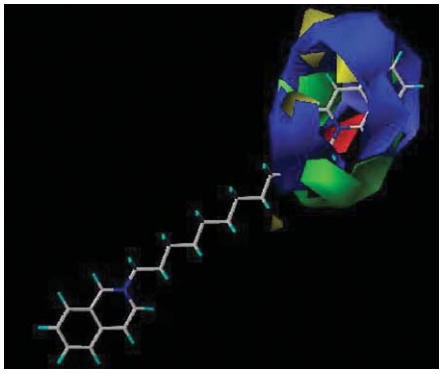
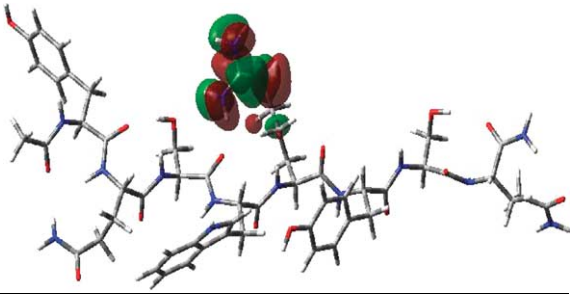


3D-QSAR study of bis-azaaromatic quaternary ammonium analogs at the blood–brain barrier choline transporter **pp 4253–4261**
Werner J. Geldenhuys, Paul R. Lockman, Tiffany H. Nguyen, Cornelis J. Van der Schyf, Peter A. Crooks, Linda P. Dwoskin and David D. Allen*

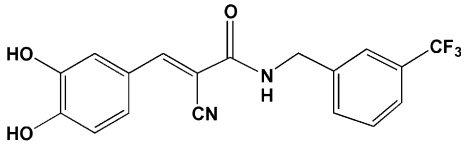


Correlation of LUMO localization with the α-amylase inhibition constant in a Tendamistat-based series of linear and cyclic peptides **pp 4262–4268**
Deborah L. Heyl,* Steve Fernandes, Leena Khullar, Jennifer Stephens, Elizabeth Blaney, Horacia Opang-Owusu, Benjamin Stahelin, Todd Pasko, Jana Jacobs, Danielle Bailey, Dennis Brown and Maria C. Milletti

Small peptides were developed based on essential binding elements of α-amylase inhibitor Tendamistat. Kinetic analysis was performed and activity was correlated with the lowest unoccupied molecular orbital (LUMO) localization in energy-minimized conformations. The positive charge/LUMO of most active inhibitors was localized on the central Arg residue of the required triplet.



Combinatorial approach to identification of tyrphostin inhibitors of cytokine signaling **pp 4269–4278**
Ling Gu, Hui Zhuang, Brian Safina, Xiao-yi Xiao, Wallace W. Bradford and Benjamin E. Rich*



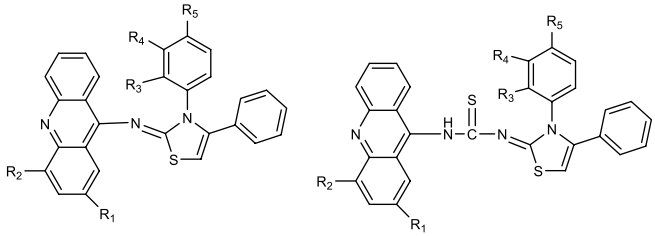
Compound **5H4**, a *meta*-trifluoromethyl derivative of tyrphostin AG490, was identified by screening a combinatorial library as a more potent inhibitor of JAK tyrosine kinase-dependent cell proliferation. The activity of **5H4** in cytokine-dependent cell lines and in lymphoma-prone IL-7 transgenic mice were examined.

Design, synthesis and evaluation of carbazole derivatives as PPARα/γ dual agonists and antioxidants **pp 4279–4290**
Rakesh Kumar, Uma Ramachandran,* Krishnamoorthy Srinivasan, Poduri Ramarao, Suryaprakash Raichur and Ranjan Chakrabarti

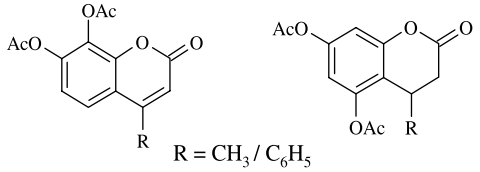
A series of hydroxycarbazole derivatives were synthesized and evaluated for PPARα/γ dual agonist as well as antioxidant activities. While most compounds showed good antioxidant activity, some compounds were identified as potential PPARα/γ dual agonists as well. Compounds **10a** and **16** were found to be active in animal studies.

Synthesis of acridinyl-thiazolino derivatives and their evaluation for anti-inflammatory, analgesic and kinase inhibition activities **pp 4291–4299**
Sham M. Sondhi,* Nirupma Singh, Anand M. Lahoti, Kiran Bajaj, Ashok Kumar, Olivier Lozach and Laurent Meijer

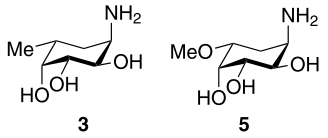
Compounds, **4a**–**o** and **5a**–**h** were synthesized by condensation of 4-phenyl-3-(2′,3′,4′(un)substituted phenyl)thiazol-2(3*H*)-imine with 9-chloro-2,4-(un)substituted acridine and 9-isothiocyanato-2,4-(un)substituted acridine, respectively. Some of these compounds exhibited good anti-inflammatory, analgesic and moderate CDK1 inhibition activities.



Mechanism of biochemical action of substituted 4-methylcoumarins. Part 11: Comparison of the specificities of acetoxy derivatives of 4-methylcoumarin and 4-phenylcoumarin to acetoxycoumarins: protein transacetylase **pp 4300–4305**
Ajit Kumar, Brajendra K. Singh, Rahul Tyagi, Sapan K. Jain, Sunil K. Sharma, Ashok K. Prasad, Hanumantharao G. Raj, Ramesh C. Rastogi, Arthur C. Watterson and Virinder S. Parmar*



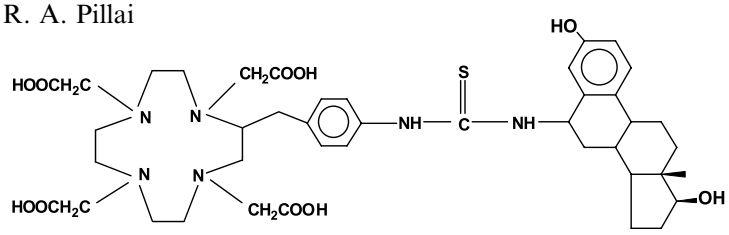
Design and synthesis of glycosidase inhibitor 5-amino-1,2,3,4-cyclohexanetetrol derivatives from (−)-*vibo*-quercitol **pp 4306–4314**
Seiichiro Ogawa,* Miwako Asada, Yoriko Ooki, Midori Mori, Masayoshi Itoh and Takashi Korenaga



3 5

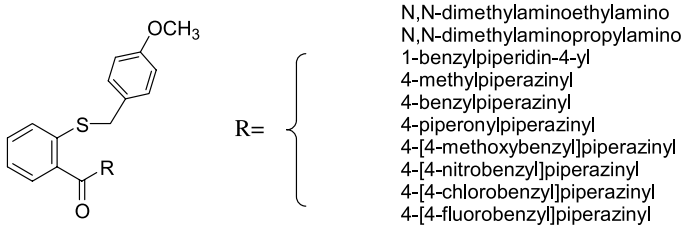
5-Amino-5-deoxy-1-*O*-methyl-L-*talo*-quercitol (**5**), an analogue of strong α-fucosidase inhibitor 5a-carba-fucopyranosylamine (**3**), was synthesized and shown to be a moderate α-fucosidase inhibitor.

An estradiol-conjugate for radiolabelling with ^{177}Lu: an attempt to prepare a radiotherapeutic agent **pp 4315–4322**
Sharmila Banerjee,* Tapas Das, Sudipta Chakraborty, Grace Samuel, Aruna Korde, Meera Venkatesh and M. R. A. Pillai

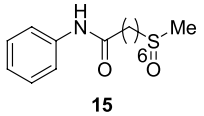


A novel approach towards the preparation of a radiolabelled steroidal–BFCA conjugate via coupling of 6α-amino-17β-estradiol with a C-functionalized DOTA derivative viz. *p*-thiocyanato-benzyl-DOTA is reported. The conjugate has been radiolabelled with ^{177}Lu, a promising therapeutic radionuclide and its preliminary biological behaviour has been studied.

Design, synthesis, and biological testing of thiosalicylamides as a novel class of calcium channel blockers **pp 4323–4331**
Ahmed S. Mehanna* and Jin Yung Kim



Design and synthesis of non-hydroxamate histone deacetylase inhibitors: identification of a selective histone acetylating agent **pp 4332–4342**
Takayoshi Suzuki,* Azusa Matsuura, Akiyasu Kouketsu, Shinya Hisakawa, Hidehiko Nakagawa and Naoki Miyata*

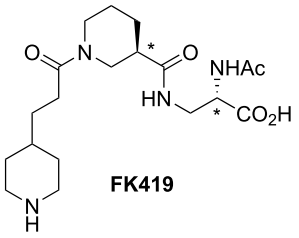


15

A series of non-hydroxamate compounds was designed, and synthesized as histone deacetylase (HDAC) inhibitors. In this series, compound **15** inhibited HDACs in vitro and caused the accumulation of acetylated histone H4 without inducing the accumulation of acetylated α-tubulin in HCT116 cells.

Design, synthesis, and structure–activity relationships of potent GPIIb/IIIa antagonists: discovery of FK419 **pp 4343–4352**

Toshio Yamanaka,* Mitsuru Ohkubo,* Satoru Kuroda, Hideko Nakamura, Fumie Takahashi, Toshiaki Aoki, Kayoko Mihara, Jiro Seki and Masayuki Kato

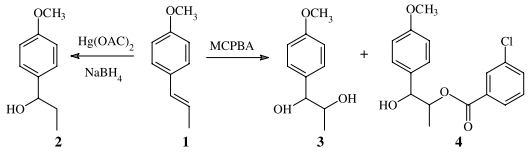


FK419

FK419 shows a safe feature of reduced prolongation of bleeding time, as well as potent inhibition of platelet aggregation.

Synthesis and antioxidant, anti-inflammatory and gastroprotector activities of anethole and related compounds **pp 4353–4358**

Rosemayre S. Freire, Selene M. Morais,* Francisco Eduardo A. Catunda-Junior and Diana C.S.N. Pinheiro



Trans-Anethole (**1**) was used as starting material to synthesize the hydroxylated derivatives (**2**), (**3**) and (**4**) and their structures were confirmed by spectral data. Hydroxyl groups were introduced on the double bond of the side chain, using *m*-chloroperbenzoic acid (MCPBA) and via oxymercuration/demercuration reactions. Anethole (**1**) and compounds (**2**), (**3**) and (**4**) were submitted to antioxidant, anti-inflammatory and gastroprotector activity tests. Compounds (**2**) and (**3**) were more active as antioxidant and anti-inflammatory agents than (**1**) and (**4**). Anethole and in lesser extent its derivatives **2** and **4** showed significant gastroprotector activity. All tested compounds do not alter significantly the total number of white blood cells.

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Instructions to contributors **pp III–VII**

*Corresponding author

ⓘ+ Supplementary data available via ScienceDirect

COVER

2005: Human liver glycogen phosphorylase A (HLGPa) is an attractive target enzyme for discovering anti-type 2 diabetes drugs. This picture shows the interaction model for a series of indole-2-carboxamides to HLGPa derived from molecular docking simulations [Liu, G.; Zhang, Z.; Luo, X.; Shen, J.; Liu, H.; Shen, X.; Chen, K.; Jiang, H. *Bioorg. Med. Chem.* **2004**, *12*, 4147–4157].

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