



Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry

journal homepage: www.elsevier.com/locate/bmc



Bioorganic & Medicinal Chemistry Volume 17, Issue 23, 2009

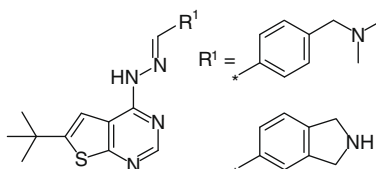
Contents

ARTICLES

Discovery of novel thieno[2,3-*d*]pyrimidin-4-yl hydrazone-based inhibitors of Cyclin D1-CDK4: Synthesis, biological evaluation and structure–activity relationships. Part 2

pp 7850–7860

Takao Horiuchi ^{*}, Motoko Nagata, Mayumi Kitagawa, Kouichi Akahane, Kouichi Uoto

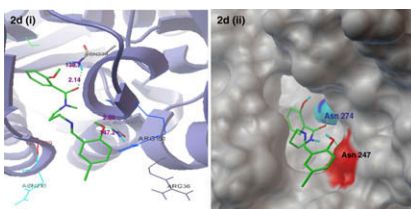


The design, synthesis and evaluation of novel thieno[2,3-*d*]pyrimidin-4-yl hydrazone analogues as CDK4 inhibitor are described. Focusing on the optimization of the heteroaryl moiety at the hydrazone with substituted phenyl groups, 4-[(methylamino)methyl]benzaldehyde (6-*tert*-butylthieno[2,3-*d*]pyrimidin-4-yl)hydrazone and 5-indolylthieno[2,3-*d*]pyrimidin-4-yl)hydrazone have been identified. The potency, selectivity profile and structure–activity relationships of our compounds are discussed.

Synthesis, antibacterial activities and molecular docking studies of peptide and Schiff bases as targeted antibiotics

pp 7861–7871

Kui Cheng, Qing-Zhong Zheng, Yong Qian, Lei Shi, Jing Zhao ^{*}, Hai-Liang Zhu ^{*}



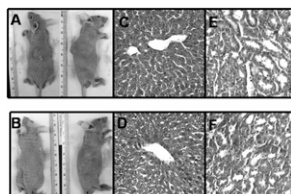
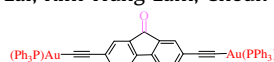
The inhibitory activities of 44 PSB against *Escherichia coli* β -ketoacyl-acyl carrier protein synthase III (ecKAS III) were investigated in vitro and molecular docking simulation also surveyed. The results demonstrate compound *N*-(3-(5-bromo-2-hydroxybenzylideneamino)propyl)-2-hydroxybenzamide (**2d**), bonding two active site of ecKAS III and fit into the mouth of the substrate tunnel, can be as a potential antibiotics agent, displaying minimal inhibitory concentration values in the range 0.39–3.13 μ g/mL against various bacteria.



Antitumor activity of diethynylfluorene derivatives of gold(I)

pp 7872–7877

Chung-Hin Chui, Raymond Siu-Ming Wong, Roberto Gambari, Gregory Yin-Ming Cheng, Marcus Chun-Wah Yuen, Kit-Wah Chan, See-Wai Tong, Fung-Yi Lau, Paul Bo-San Lai, Kim-Hung Lam, Cheuk-Lam Ho, Chi-Wai Kan ^{*}, Kelvin Sze-Yin Leung ^{*}, Wai-Yeung Wong ^{*}

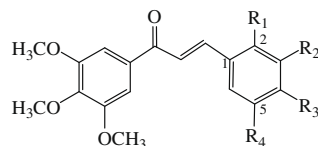


End-capping the diethynylfluorene unit with gold(I) moieties could significantly strengthen its cytotoxic activity on human cancer cells. Further study of the gold(I) derivative demonstrated its in vivo antitumor activity using Hep3B human hepatocellular carcinoma model with limited adverse effects on vital organs including liver and kidney.

Synthesis and biological evaluation of 3',4',5'-trimethoxychalcone analogues as inhibitors of nitric oxide production and tumor cell proliferation

pp 7909–7914

Yerra Koteswara Rao, Shih-Hua Fang, Yew-Min Tzeng *



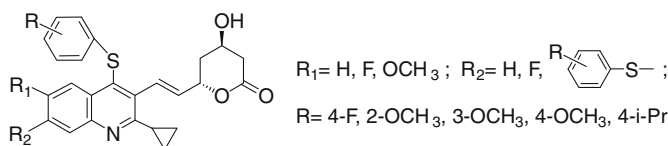
$R_1, R_2, R_3, R_4 = \text{OH and/or}$
 $\text{OCH}_3 \text{ or } \text{CH}_3 \text{ or F or Br or NO}_2$

A series of 23 3',4',5'-trimethoxychalcone analogues were synthesized and their inhibitory effects, on nitric oxide production in LPS/IFN- γ -treated macrophages, and human tumor cell proliferation has been investigated.

**Synthesis and HMG-CoA reductase inhibition of 2-cyclopropyl-4-thiophenyl-quinoline mevalonolactones**

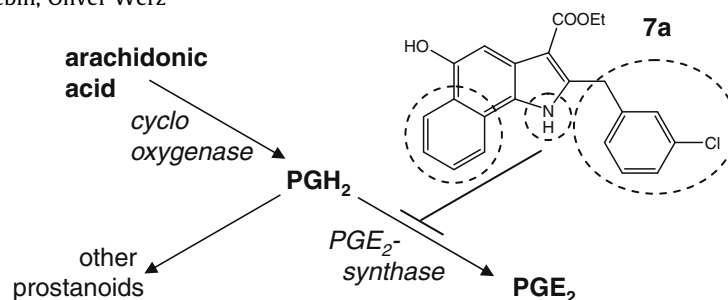
pp 7915–7923

Shikui Zhao *, Weicheng Zhou, Jun liu

**Discovery of benzo[*g*]indol-3-carboxylates as potent inhibitors of microsomal prostaglandin *E*₂ synthase-1**

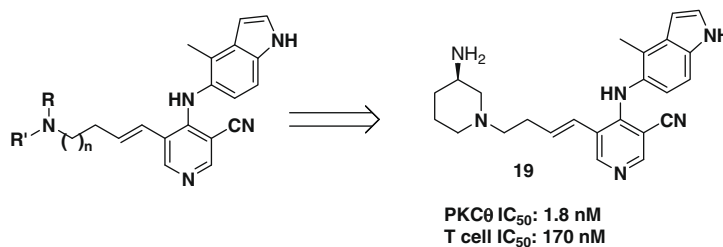
pp 7924–7932

Andreas Koeberle, Eva-Maria Haberl, Antonietta Rossi, Carlo Pergola, Friederike Dehm, Hinnak Northoff, Reinhard Troschuetz, Lidia Sautebin, Oliver Werz *

**5-Vinyl-3-pyridinecarbonitrile inhibitors of PKC θ : Optimization of enzymatic and functional activity**

pp 7933–7948

L. Nathan Tumey *, Niala Bhagirath, Agnes Brennan, Natasja Brooijmans, Julie Lee, Xiaoke Yang, Diane H. Boschelli



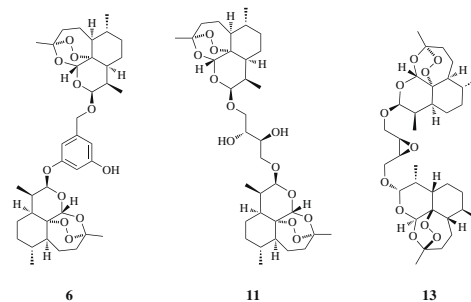
We describe the optimization of enzymatic and cellular potency of a series of 5-vinyl-3-pyridinecarbonitrile inhibitors of PKC θ .

Antiprotozoal, anticancer and antimicrobial activities of dihydroartemisinin acetal dimers and monomers

pp 7949–7957

Desmond Slade^{*}, Ahmed M. Galal, Waseem Gul, Mohamed M. Radwan, Safwat A. Ahmed, Shabana I. Khan, Babu L. Tekwani, Melissa R. Jacob, Samir A. Ross, Mahmoud A. ElSohly^{*}

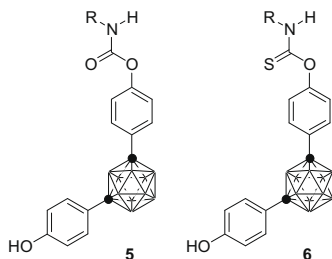
Nine dihydroartemisinin acetal dimers with diversely functionalized linker units were synthesized and tested for in vitro antiprotozoal, anticancer and antimicrobial activity. Full spectroscopic data are given for the title compounds.



Novel estrogen receptor (ER) modulators: Carbamate and thiocarbamate derivatives with *m*-carborane bisphenol structure

pp 7958–7963

Kiminori Ohta, Takumi Ogawa, Tomoharu Suzuki, Shigeru Ohta, Yasuyuki Endo^{*}

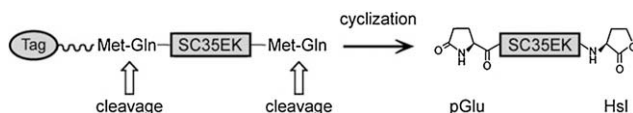


Novel carborane-containing estrogen receptor (ER) modulators, carbamates and thiocarbamates derivatives **5** and **6**, were designed and synthesized based upon the structure of *m*-carborane bisphenol skeleton. Thiocarbamates **6** showed more potent estrogenic activity than the carbamates **5**.

Bioorganic synthesis of a recombinant HIV-1 fusion inhibitor, SC35EK, with an N-terminal pyroglutamate capping group

pp 7964–7970

Kazumi Kajiwar, Kentaro Watanabe, Rei Tokiwa, Tomoko Kurose, Hiroaki Ohno, Hiroko Tsutsumi, Yoji Hata, Kazuki Izumi, Eiichi Kodama, Masao Matsuoka, Shinya Oishi^{*}, Nobutaka Fujii^{*}



An anti-HIV peptide with N- and C-terminal end-capping groups was synthesized by cyanogen bromide-mediated cleavage of a recombinant protein.

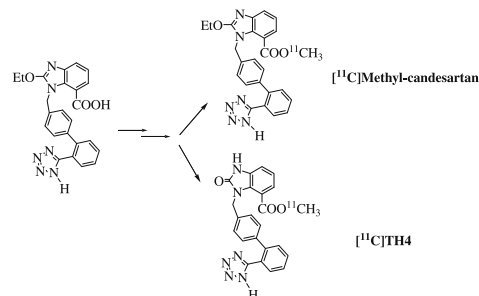


Novel O-[¹¹C]methylated derivatives of candesartan as angiotensin II AT₁ receptor imaging ligands: Radiosynthesis and ex vivo evaluation in rats

pp 7971–7977

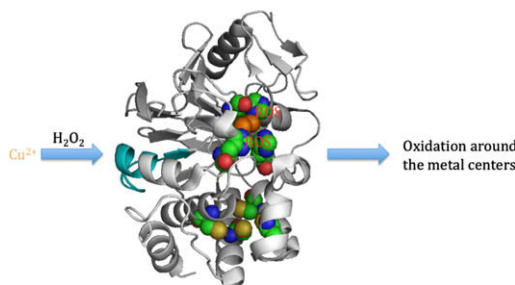
Tayebeh Hadizad, Sheryn A. Kirkpatrick, Samantha Mason, Kevin Burns, Rob. S. Beanlands, Jean N. DaSilva^{*}

Two novel radiotracers ([¹¹C]methyl-candesartan and its desethyl derivative ([¹¹C]TH4)) were synthesized via ¹¹C-methylation of the tetrazole-protected candesartan as potential imaging agents for angiotensin II AT₁ receptors.

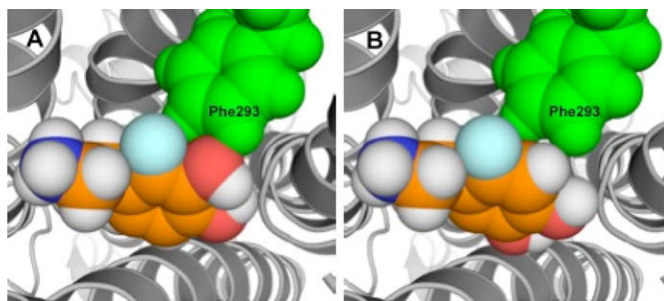


Oxidatively induced Cu for Mn exchange in protein phosphatase 1 γ : A new method for active site analysis

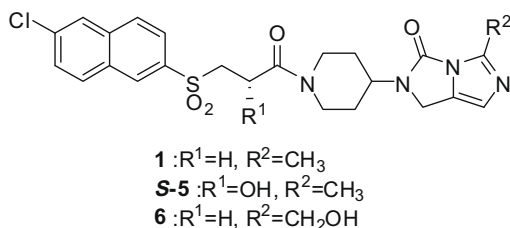
pp 7978–7986

Atsushi Miyazaki, Magne O. Sydnes, Minoru Isobe^{*}, Hiroshi Ohinata, Motoi Miyazu, Akira Takai**Structural basis of the selectivity of the β_2 -adrenergic receptor for fluorinated catecholamines**

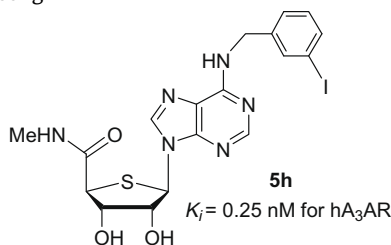
pp 7987–7992

Chaya Pooput, Erica Rosemond, Joel Karpiak, Francesca Deflorian, Santiago Vilar, Stefano Costanzi, Jürgen Wess, Kenneth L. Kirk^{*}The binding modes of 2FNE and 6FNE at the N293F mutant β_2 -adrenergic receptor.**Synthesis and biological evaluation of the metabolites of 2-(1-{3-[(6-chloronaphthalen-2-yl)sulfonyl]propanoyl}piperidin-4-yl)-5-methyl-1,2-dihydro-3H-imidazo[1,5-c]imidazol-3-one**

pp 7993–8002

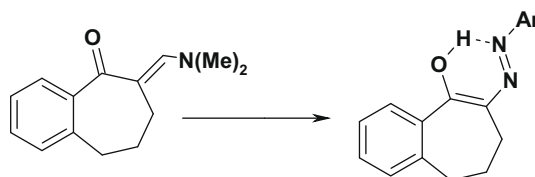
Takuya Fujimoto^{*}, Mamoru Tobisu, Noriko Konishi, Masaki Kawamura, Norio Tada, Terufumi Takagi, Keiji KuboSynthesis and biological evaluation of the metabolites of our Factor Xa inhibitor **1** were performed, and the active metabolites **5-5** and **6** with the potent activity comparable to that of **1** were identified.**Design and synthesis of N^6 -substituted-4'-thioadenosine-5'-uronamides as potent and selective human A_3 adenosine receptor agonists**

pp 8003–8011

Won Jun Choi, Hyuk Woo Lee, Hea Ok Kim, Moshe Chinn, Zhan-Guo Gao, Amit Patel, Kenneth A. Jacobson, Hyung Ryong Moon, Young Hoon Jung, Lak Shin Jeong^{*}The structure–activity relationship of N^6 -substituted-4'-thioadenosine-5'-uronamides (**5h**, $K_i = 0.25 \text{ nM}$) as potent human A_3 adenosine receptor agonists is reported.

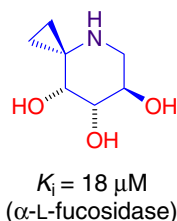
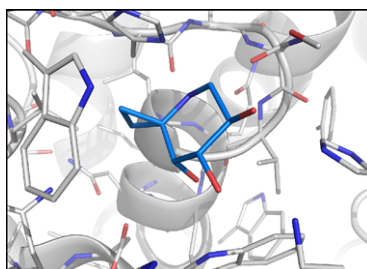
Synthesis, tautomerism, and antimicrobial, anti-HCV, anti-SSPE, antioxidant, and antitumor activities of arylazobenzosuberones

pp 8012–8019

Thoraya A. Farghaly^{*}, Mohamed M. Abdalla

The spirocyclopropyl moiety as a methyl surrogate in the structure of L-fucosidase and L-rhamnosidase inhibitors

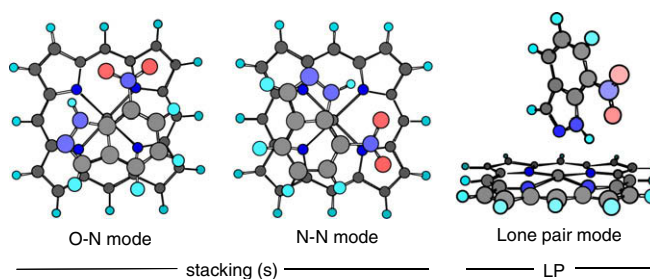
pp 8020–8026

Morwenna S. M. Pearson, Nicolas Floquet, Claudia Bello, Pierre Vogel, Richard Plantier-Royon, Jan Szymoniak, Philippe Bertus, Jean-Bernard Behr^{*}

Nitrogen-in-the-ring analogues of L-fucose and L-rhamnose, which feature a spirocyclopropyl moiety in place of the methyl group of the natural sugar, were prepared and assayed.

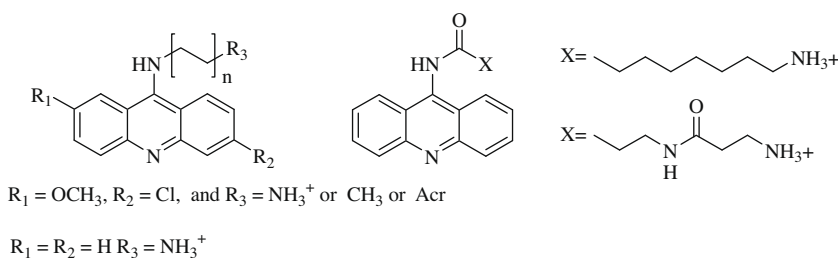
Theoretical calculations of a model of NOS indazole inhibitors: Interaction of aromatic compounds with Zn-porphyrins

pp 8027–8031

José Elguero^{*}, Ibon Alkorta, Rosa M. Claramunt, Concepción López, Dionisia Sanz, Dolores Santa María

Antimalarial acridines: Synthesis, in vitro activity against P. falciparum and interaction with hemozoin

pp 8032–8039

Lucie Guetzoyan, Xiao-Min Yu, Florence Ramiandrasoa, Stéphanie Pethe, Christophe Rogier, Bruno Pradines, Thierry Cresteil, Martine Perrée-Fauvet, Jean-Pierre Mahy^{*}

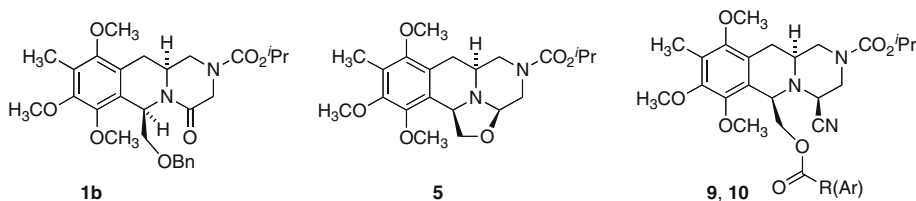
Synthesis of new 9-aminoacridines and evaluation of in vitro anti-malarial activity. Inhibitory effect on haem crystallization.



Cytotoxicity mechanisms of pyrazino[1,2-*b*]isoquinoline-4-ones and SAR studies

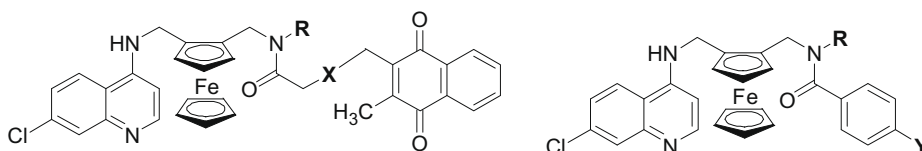
pp 8040–8047

Irene Ortín, Juan Francisco González, Elena de la Cuesta, Cristina Manguan-García, Rosario Perona, Carmen Avendaño *

**Antimalarial activities of ferroquine conjugates with either glutathione reductase inhibitors or glutathione depletors via a hydrolyzable amide linker**

pp 8048–8059

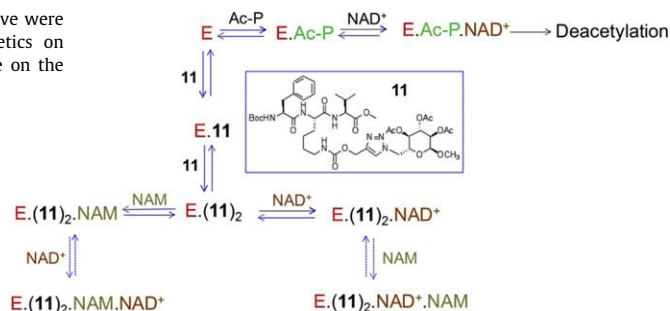
Natascha Chavain *, Elisabeth Davioud-Charvet, Xavier Trivelli, Linda Mbeki, Matthias Rottmann, Reto Brun, Christophe Biot *

**Development and characterization of lysine based tripeptide analogues as inhibitors of Sir2 activity**

pp 8060–8072

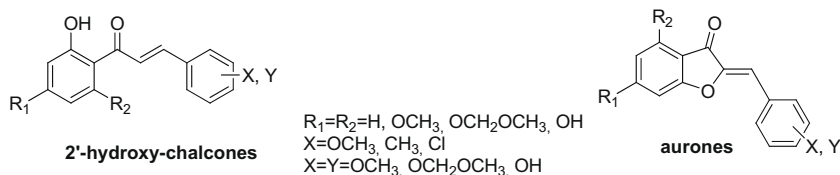
Subhra Prakash Chakrabarty, Ramesh Ramapanicker, Roli Mishra, Srinivasan Chandrasekaran, Hemalatha Balaran *

Peptides containing a lysine residue protected at the ϵ -amino group as an alkyne derivative were functionalized with azides of sugars/thymidine using click chemistry. Inhibition kinetics on *Plasmodium falciparum* Sir2 using the peptide conjugates established a dual binding site on the enzyme.

**Natural and synthetic 2'-hydroxy-chalcones and aurones: Synthesis, characterization and evaluation of the antioxidant and soybean lipoxygenase inhibitory activity**

pp 8073–8085

Anastasia Detsi *, Maya Majdalani, Christos A. Kontogiorgis, Dimitra Hadjipavlou-Litina, Panagiotis Kefalas

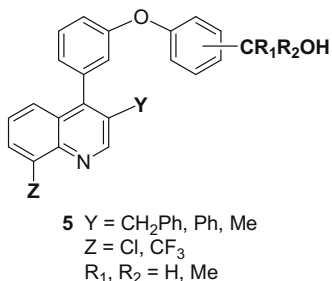


Naturally occurring and synthetic flavonoids belonging to the 2'-hydroxy-chalcone and aurone families, have been synthesized and tested for their antioxidant and soybean lipoxygenase inhibitory activity.

4-(3-Aryloxyaryl)quinoline alcohols are liver X receptor agonists

pp 8086–8092

Ronald C. Bernotas^{*}, David H. Kaufman, Robert R. Singhaus, John Ullrich, Rayomand Unwalla, Elaine Quinet, Ponnal Nambi, Anna Wilhelmsson, Annika Goos-Nilsson, Jay Wrobel

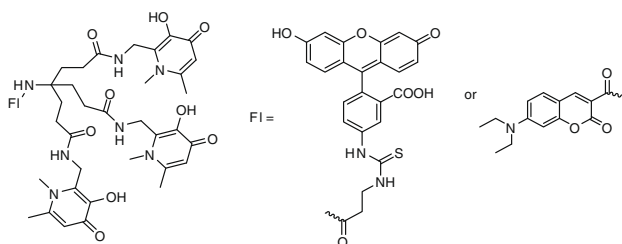


A series of 4-(3-aryloxyaryl)quinolines **5** was prepared as LXR agonists.

The selective quantification of iron by hexadentate fluorescent probes

pp 8093–8101

Yong Min Ma, Robert C. Hider^{*}



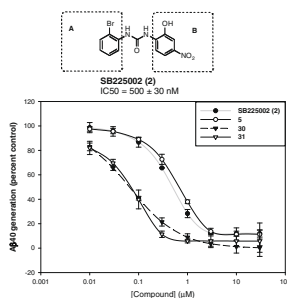
Coumarin or fluorescein-based hexadentate probes for iron selective quantification is described.



Structural optimization of a CXCR2-directed antagonist that indirectly inhibits γ -secretase and reduces A β

pp 8102–8112

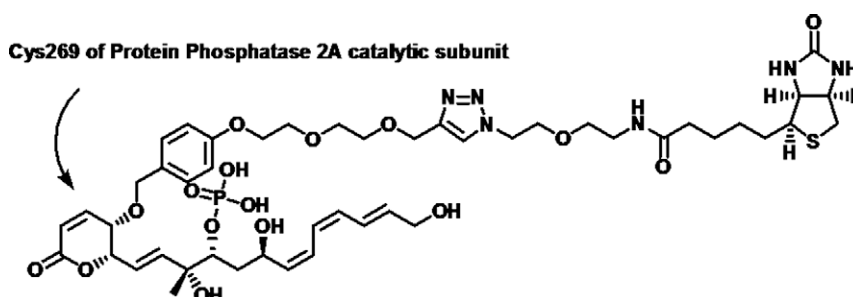
Pancham Bakshi^{*}, Chao Jin, Pierre Broutin, Beniam Berhane, Jon Reed, Michael Mullan



Antitumor antibiotic fostriecin covalently binds to cysteine-269 residue of protein phosphatase 2A catalytic subunit in mammalian cells

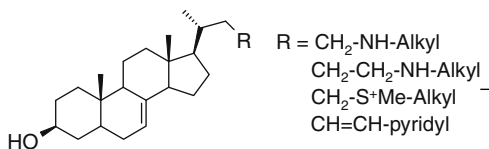
pp 8113–8122

Toshifumi Takeuchi, Noriyuki Takahashi, Kazutomo Ishi, Tomoe Kusayanagi, Kouji Kuramochi, Fumio Sugawara^{*}




Side chain azasteroids and thiasteroids as sterol methyltransferase inhibitors in ergosterol biosynthesis**pp 8123–8137**

Delphine Renard, Johann Perruchon, Martin Giera, Jörg Müller, Franz Bracher *



Novel antifungal Δ^7 -azasteroids and thiasteroids were prepared as inhibitors of the enzyme Δ^24 -sterol methyltransferase (24-SMT).

*Corresponding author

 Supplementary data available via ScienceDirect

COVER

Side chain azasteroids and thiasteroids as sterol methyltransferase inhibitors in ergosterol biosynthesis: an abstracted close-up photo of an agardiltution test with the model organism *Yarrowia lipolytica* overlaid by the three-dimensional structures of the sterols zymosterol, fecosterol, cholesta-5,7,24-trien-3 β -ol and substance 19 (upper right corner) - a sterol methyltransferase (SMT) inhibitor is shown. The substance cholesta-5,7,24-trien-3 β -ol (lower right) is the major sterol which is found in the unsaponifiable matter of the test organism, when the transformation of zymosterol (lower left) to fecosterol (upper left) by the SMT is inhibited. [Renard, D.; Perruchon, J.; Giera, M.; Müller, J.; Bracher, F. *Bioorg. Med. Chem.* **2009**, 17, 8123].

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ISSN 0968-0896