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# Bioorganic & Medicinal Chemistry

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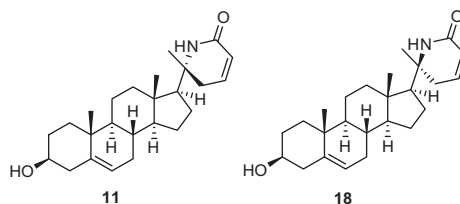
## Bioorganic & Medicinal Chemistry Volume 18, Issue 19, 2010

### Contents

#### ARTICLES

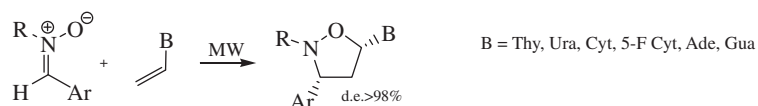
#### 20-Aminosteroids as a novel class of selective and complete androgen receptor antagonists and inhibitors of prostate cancer cell growth pp 6960–6969

Manolis A. Foustieris, Undine Schubert, Daniela Roell, Julia Roediger, Nikolaos Bailis, Sotiris S. Nikolaropoulos, Aria Baniahmad\*, Athanassios Giannis\*



#### Synthesis and biological evaluation of diastereoisomerically pure *N,O*-nucleosides pp 6970–6976

Olga Bortolini\*, Antonio De Nino, Tommaso Eliseo, Riccardo Gavioli, Loredana Maiuolo\*, Beatrice Russo, Fabio Sforza

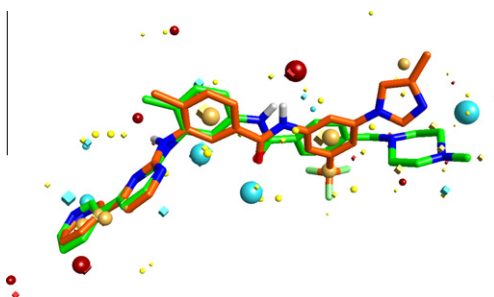


The synthesis of some new *N,O*-nucleosides is described, based on the 1,3-dipolar cycloaddition of nitrones and unprotected vinyl nucleobases. Promising results were found during their biological evaluation.



#### Structural resemblances and comparisons of the relative pharmacological properties of imatinib and nilotinib pp 6977–6986

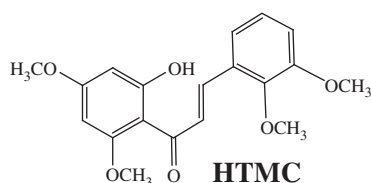
Paul W. Manley\*, Nikolaus Stiefl, Sandra W. Cowan-Jacob, Susan Kaufman, Jürgen Mestan, Markus Wartmann, Marion Wiesmann, Richard Woodman, Neil Gallagher



### Identification of small molecule inhibitors of telomerase activity through transcriptional regulation of hTERT and calcium induction pathway in human lung adenocarcinoma A549 cells

pp 6987–6994

Yerra Koteswara Rao, Te-Yu Kao, Ming-Fang Wu, Jiunn-Liang Ko\*, Yew-Min Tzeng\*



Among tested, HTMC was the most potent that inhibited telomerase activity, expression of hTERT and hTERT promoter in A549 cells. HTMC treatment also reduced colony formation of A549 cells. The release of  $\text{Ca}^{2+}$  was the underlying mechanisms of suppressed telomerase activity and hTERT transcription in A549 cells exposed to HTMC.

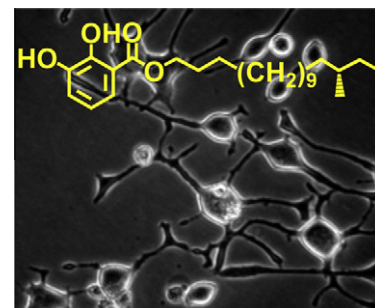


### Gentisides C–K: Nine new neuritogenic compounds from the traditional Chinese medicine *Gentiana rigescens* Franch

pp 6995–7000

Lijuan Gao, Lan Xiang, Yan Luo, Guangfa Wang, Jinyou Li, Jianhua Qi\*

Gentisides C–K are additional members of a novel class of neuritogenic compounds. They exhibited significant neuritogenic activity against PC12 cells. The structure–activity relationships within the gentisides A–K revealed that the alkyl chain length is important for the activity, but structure diversity at the end of alkyl chain is not.

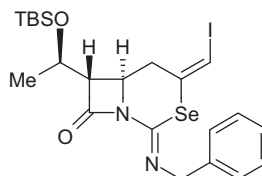


### Identification of organoselenium compounds that possess chemopreventive properties in human prostate cancer LNCaP cells

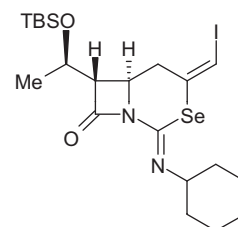
pp 7001–7008

Riyako Terazawa, Dinesh R. Garud, Nanako Hamada, Yasunori Fujita, Tomohiro Itoh, Yoshinori Nozawa, Keita Nakane, Takashi Deguchi, Mamoru Koketsu, Masafumi Ito\*

Two organoselenium compounds possess chemopreventive properties in human prostate cancer LNCaP cells.



3-Selena-1-dethiacephem 13



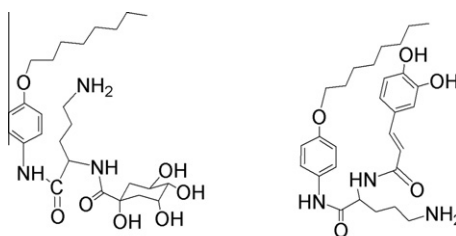
3-Selena-1-dethiacephem 14



### Synthesis, anti-fungal and 1,3-β-D-glucan synthase inhibitory activities of caffeic and quinic acid derivatives

pp 7009–7014

Chao-Mei Ma\*, Takashi Abe, Tadazumi Komiyama, Wei Wang, Masao Hattori\*, Mohsen Daneshtalab



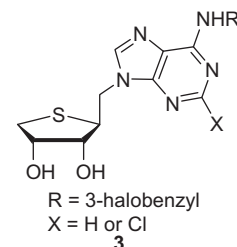
Anti-fungal and inhibitory on 1,3-glucan synthase



## Design, synthesis, and binding of homologated truncated 4'-thioadenosine derivatives at the human A<sub>3</sub> adenosine receptors pp 7015–7021

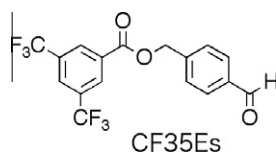
Hyuk Woo Lee, Hea Ok Kim, Won Jun Choi, Sun Choi, Jin Hee Lee, Seul-gi Park, Lena Yoo, Kenneth A. Jacobson, Lak Shin Jeong\*

The homologated derivatives **3** in which a methylene group was inserted into the glycosidic bond of truncated 4'-thioadenosine were synthesized as potential human A<sub>3</sub> adenosine receptor antagonists.



## Retinobenzaldehydes as proper-trafficking inducers of folding-defective P23H rhodopsin mutant responsible for Retinitis Pigmentosa pp 7022–7028

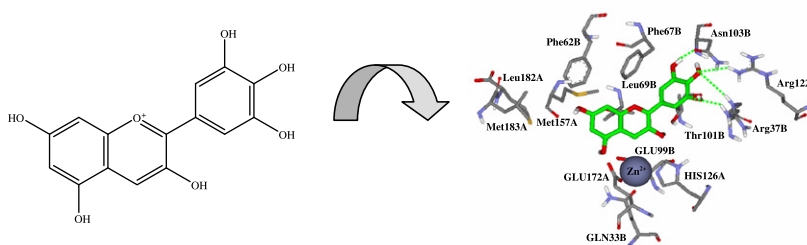
Kenji Ohgane\*, Kosuke Dodo, Yuichi Hashimoto



The design and synthesis of a class of stable nonpolyene-type rhodopsin ligands which induce folding/trafficking of P23H rhodopsin are described.

## Delphinidin, a dietary anthocyanidin in berry fruits, inhibits human glyoxalase I pp 7029–7033

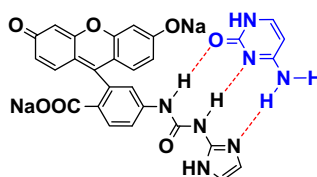
Ryoko Takasawa, Kazunori Saeki, Akinobu Tao, Atsushi Yoshimori, Hiromi Uchiro, Mutsunori Fujiwara, Sei-ichi Tanuma\*



The structure of delphinidin and its predicted binding mode on the human GLO I

## A fluorescein-containing, small-molecule, water-soluble receptor for cytosine free bases pp 7034–7042

Yu Lin Jiang\*, Puneet Patel, Suzane M. Klein



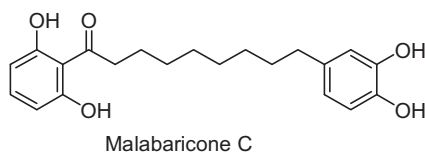
A fluorescein-containing, small-molecule, water-soluble, ureido receptor has been synthesized. The binding with cytosine free bases was investigated using <sup>15</sup>N NMR and fluorescence spectroscopies.



**Comparative nuclease and anti-cancer properties of the naturally occurring malabaricones**

pp 7043–7051

Birija S. Patro, Mrityunjay Tyagi, Jayati Saha, Subrata Chattopadhyay\*

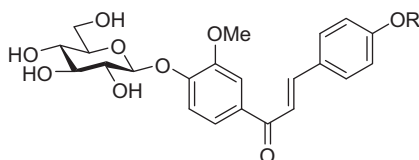


Consistent with its Cu(II)-mediated nuclease property, mal C could efficiently ( $IC_{50} \sim 5 \mu M$ ) induce killing of the MCF-7 human breast cancer cell line via oxidative damage to cellular DNA.

**Chalcone glycosides isolated from aerial parts of *Brassica rapa* L. 'hidabeni' suppress antigen-stimulated degranulation in rat basophilic leukemia RBL-2H3 cells**

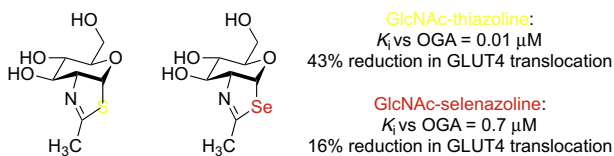
pp 7052–7057

Tomohiro Itoh, Masayuki Ninomiya, Yoshinori Nozawa, Mamoru Koketsu\*

R = H; 4'-O- $\beta$ -D-Glucopyranosyl-4-hydroxy-3'-methoxychalcone (**C1**)R = Me; 4'-O- $\beta$ -D-Glucopyranosyl-3',4-dimethoxychalcone (**C2**)**OGA inhibition by GlcNAc-selenazoline**

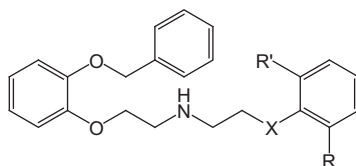
pp 7058–7064

Eun Ju Kim, Dona C. Love, Etzer Darout, Mohannad Abdo, Brian Rempel, Stephen G. Withers, Paul R. Rablen, John A. Hanover\*, Spencer Knapp\*

**Structure–activity relationships in 1,4-benzodioxan-related compounds. 10. Novel  $\alpha_1$ -adrenoreceptor antagonists related to openphendioxan: Synthesis, biological evaluation, and  $\alpha_{1d}$  computational study**

pp 7065–7077

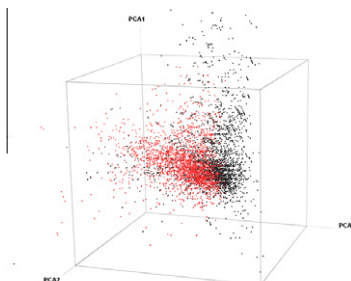
Antonio Carrieri\*, Alessandro Piergentili, Fabio Del Bello, Mario Giannella, Maria Pigini, Amedeo Leonardi, Francesca Fanelli, Wilma Quaglia\*



**QSAR-based solubility model for drug-like compounds**

pp 7078–7084

Rafael Gozalbes\*, Antonio Pineda-Lucena\*

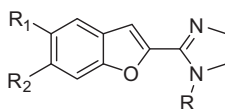


A QSAR model for predicting the solubility of drug-like compounds has been developed based on simple 1D and 2D descriptors. The model does not require any experimentally determined value and it is intended to be used as a decision tool when selecting compounds for drug discovery campaigns.

**Novel imidazoline compounds as partial or full agonists of D<sub>2</sub>-like dopamine receptors inspired by I<sub>2</sub>-imidazoline binding sites ligand 2-BFI**

pp 7085–7091

Gianfabio Giorgioni\*, Dario Ambrosini, Cristian Vesprini, Alan Hudson, Cinzia Nasuti, Antonio Di Stefano, Piera Sozio, Osele Ciampi, Barbara Costa, Claudia Martini, Antonio Carrieri, Giuseppe Carbonara, Christoph Enzensperger, Maria Pignini

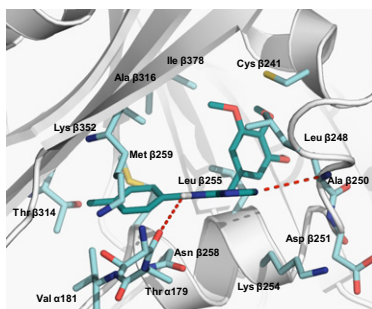


Based on the well known biological versatility of the imidazoline nucleus, we prepared the novel derivatives **3a–k** inspired by 2-BFI scaffold to assess imidazoline molecules as D<sub>2</sub>-like dopamine receptor ligands. Conservative chemical modifications of the lead structure, such as the introduction of an hydroxy group in the aromatic ring alone or associated with *N*-benzyl substitution, provided partial (**3f**) or nearly full (**3e** and **3h**) agonists, all endowed with D<sub>2</sub>-like potency comparable to that of dopamine.

**Structure-based virtual screening of novel tubulin inhibitors and their characterization as anti-mitotic agents**

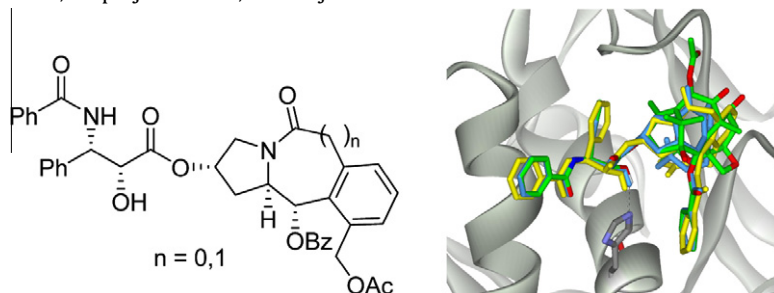
pp 7092–7100

Nam Doo Kim, Eun-Sook Park, Young Hoon Kim, Seung Kee Moon, Sung Sook Lee, Soon Kil Ahn, Dae-Yeul Yu, Kyoung Tai No\*, Kyun-Hwan Kim\*

**Design and synthesis of de novo cytotoxic alkaloids by mimicking the bioactive conformation of paclitaxel**

pp 7101–7112

Liang Sun, Jean M. Veith, Paula Pera, Ralph J. Bernacki, Iwao Ojima\*



Design, syntheses and biological evaluations of de novo paclitaxel mimics are reported.

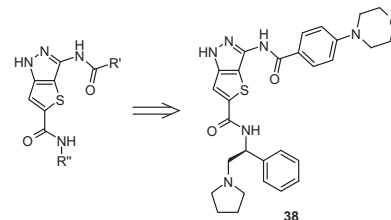


### Thieno[3,2-c]pyrazoles: A novel class of Aurora inhibitors with favorable antitumor activity

pp 7113–7120

Simona Bindi\*, Daniele Fancelli, Cristina Alli, Daniela Berta, Jay A. Bertrand, Alexander D. Cameron, Paolo Cappella, Patrizia Carpinelli, Giovanni Cervi, Valter Croci, Matteo D'Anello, Barbara Forte, M. Laura Giorgini, Aurelio Marsiglio, Juergen Moll, Enrico Pesenti, Valeria Pittalà, Maurizio Pulici, Federico Riccardi-Sirtori, Fulvia Roletto, Chiara Soncini, Paola Storici, Mario Varasi, Daniele Volpi, Paola Zugnoni, Paola Vianello

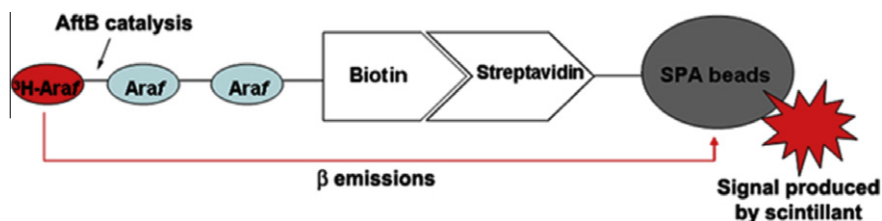
In this paper we report on the optimization of the thieno[3,2-c]pyrazole series as inhibitors of the Aurora kinases to give a promising lead compound endowed with high potency in in vitro assays and active in vivo in the HL-60 xenograft tumor model.



### Development of a plate-based scintillation proximity assay for the mycobacterial AftB enzyme involved in cell wall arabinan biosynthesis

pp 7121–7131

Jian Zhang, Anita G. Amin, Alexandra Hölemann, Peter H. Seeberger, Delphi Chatterjee\*



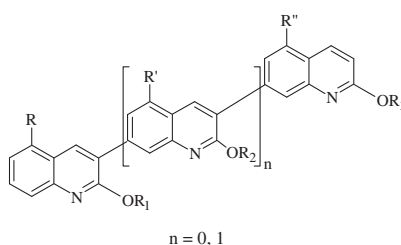
Several oligosaccharide acceptors mimicking segments of mycobacterial arabinan were successfully synthesized and used in cell free assays. The enzymatic products formed were identified as  $\beta$ -(1→2) arabinofuranose adducts—a function of AftB. Among these, the biotinylated disaccharide was further used to develop a scintillation proximity assay.



### Synthesis and biological activities of new di- and trimeric quinoline derivatives

pp 7132–7143

Sidonie Broch, Hélène Hénon, Anne-Laure Debaud, Marie-Laure Fogeron, Nathalie Bonnefoy-Bérard, Fabrice Anizon, Pascale Moreau\*



### OTHER CONTENT

#### Corrigendum

p 7144

\*Corresponding author

Supplementary data available via ScienceDirect

**COVER**

The cover picture shows the first steroid that acts as complete and selective androgen receptor antagonist. This novel 20-aminosteroid derivative inhibits prostate cancer cell growth by induction of cellular senescence, which is represented by the old, but still alive plant on the edge of a cliff [Fousteris, M. A.; Schubert, U.; Roell, D.; Roediger, J.; Bailis, N.; Nikolaropoulos, S. S.; Baniahmad, A.; Giannis, A. *Bioorg. Med. Chem.* **2010**, 18, 6960–6969].

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ISSN 0968-0896