

## Contents

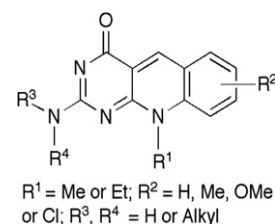
### ARTICLES

**Antitumor studies. Part 3: Design, synthesis, antitumor activity, and molecular docking study of novel 2-methylthio-, 2-amino-, and 2-(*N*-substituted amino)-10-alkyl-2-deoxo-5-deazaflavins**

Hamed I. Ali, Noriyuki Ashida and Tomohisa Nagamatsu\*

pp 6336–6352

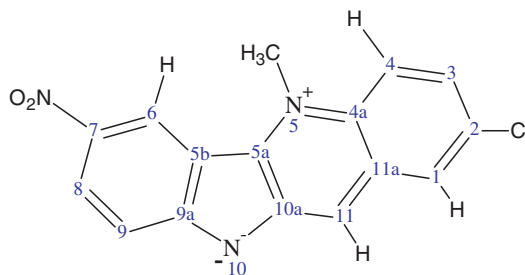
Some of the prepared 2-amino- and 2-(substituted amino)-10-alkyl-2-deoxo-5-deazaflavins exhibited significant antitumor activities against CCRF-HSB-2 and KB cells. A good correlation between the IC<sub>50</sub> and binding free energy by docking into PTK (pdb code:1t46) for the 5-deazaflavins was obtained.



**Synthesis of cryptolepine analogues as potential bioreducible anticancer agents**

Scott Seville,\* Roger M. Phillips, Steven D. Shnyder and Colin W. Wright

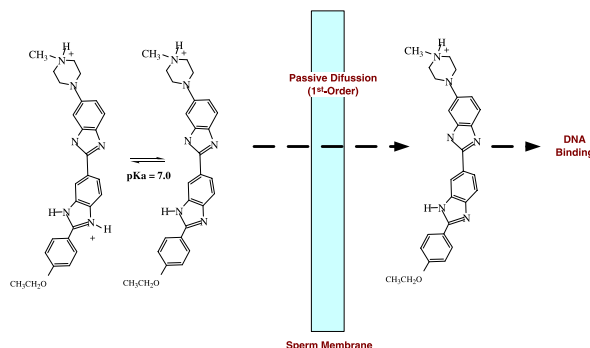
pp 6353–6360



**Mass transport kinetics of the DNA-binding dye Hoechst-33342 into bovine spermatozoa**

Robert B. Weisenfeld\*

pp 6361–6366

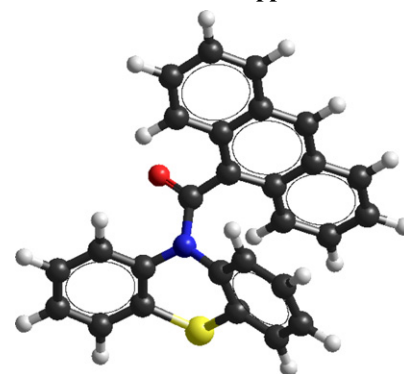


### Selective reversible inhibition of human butyrylcholinesterase by aryl amide derivatives of phenothiazine

pp 6367–6378

Sultan Darvesh,\* Robert S. McDonald, Katherine V. Darvesh, Diane Mataija, Sarah Conrad, Geraldine Gomez, Ryan Walsh and Earl Martin

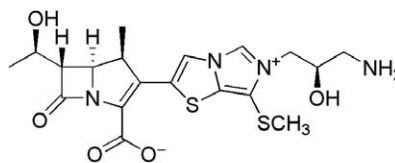
Synthesized *N*-(10)-aromatic amides of phenothiazine were specific butyrylcholinesterase inhibitors. Molecular volumes, steric and electronic factors contributed to specificity and potency. Inhibition constants in the nanomolar range were achieved and computed log *P* values indicated high potential for inhibiting brain butyrylcholinesterase.



### CP5484, a novel quaternary carbapenem with potent anti-MRSA activity and reduced toxicity

pp 6379–6387

Takahisa Maruyama,\* Yasuo Yamamoto, Yuko Kano, Mizuyo Kurazono, Eiji Matsuhisa, Hiromi Takata, Toshihiko Takata, Kunio Atsumi, Katsuyoshi Iwamatsu and Eiki Shitara



CP5484

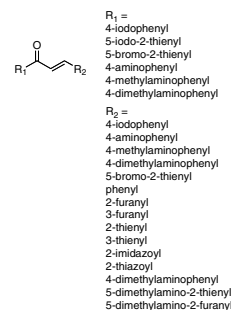
A new series of 1 $\beta$ -methyl carbapenems possessing a 6,7-disubstituted imidazo[5,1-*b*]thiazol-2-yl group was prepared. Among them **CP5484** showed potent anti-MRSA activity with reduced acute toxicity in mice. Further evaluation of **CP5484** is also reported.

### Structure–activity relationship of chalcones and related derivatives as ligands for detecting of $\beta$ -amyloid plaques in the brain

pp 6388–6396

Masahiro Ono,\* Miyuki Hori, Mamoru Haratake, Takami Tomiyama, Hiroshi Mori and Morio Nakayama

Synthesis, SAR and biodistribution of novel chalcone and chalcone-like compounds for  $\beta$ -amyloid imaging agents are reported.

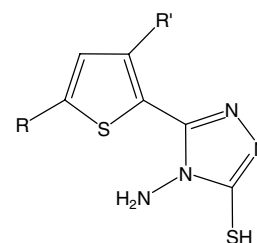


### A novel approach to cyclin-dependent kinase 5/p25 inhibitors: A potential treatment for Alzheimer's disease

pp 6397–6406

Mahendra Ramesh Shiradkar,\* Mallikarjuna Bandrehally Padhalingappa, Sastry Bhetalabhotla, Kalyan Chakravarthy Akula, Dattu Anna Tupe, Raghotham Reddy Pinninti and Suman Thummanagoti

The synthesis of a new series of thienyl triazole derivatives under microwave assisted organic synthesis is described. They were tested as cdk5/p25 inhibitors. It was also observed that compounds **4**, **5**, **7** and **8** from series I while **13**, **14**, **16** and **17** from series II emerged as significant cdk5/p25 inhibitors. Few compounds were good inhibitors while others were inactive.

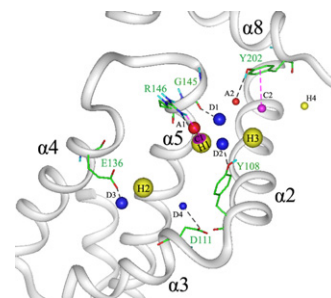


### Construction of a three-dimensional pharmacophore for Bcl-2 inhibitors by flexible docking and the multiple copy simultaneous search method

pp 6407–6417

Can-Hui Zheng, You-Jun Zhou,\* Ju Zhu, Hai-Tao Ji, Jun Chen, Yao-Wu Li, Chun-Quan Sheng, Jia-Guo Lu, Jun-Hang Jiang, Hui Tang and Yun-Long Song

A three-dimensional pharmacophore model for Bcl-2 inhibitors was constructed based on the binding modes of the representative inhibitors determined by flexible docking. Then, the distances between pharmacophoric points were optimized on the basis of the most energetically favorable minima of functional groups with similar features to these pharmacophoric points, which determined by the MCSS method.

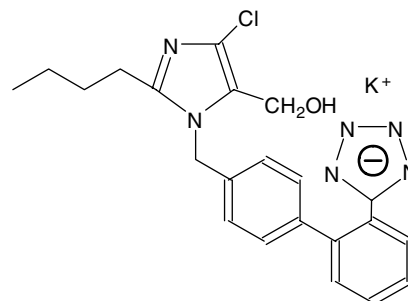


### Losartan and its interaction with copper(II): Biological effects

pp 6418–6424

Susana B. Etcheverry, Evelina G. Ferrer, Luciana Naso, Daniel A. Barrio, Luis Lezama, Teófilo Rojo and Patricia A. M. Williams\*

Losartan potassium salt and its copper complex  $[\text{Cu}(\text{Los})_2(\text{H}_2\text{O})_3]_2$  were tested in osteoblastic culture. It has been demonstrated that Losartan is harmless for normal and tumoral bone cells while the copper complex inhibited cell proliferation in a dose response manner. Besides, Losartan did not exert antioxidant properties or caused morphological alterations in the cells. On the contrary, its copper(II) complex produced strong morphological changes and exhibited moderate antioxidant behavior.



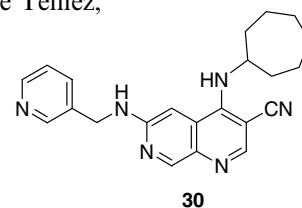
### Identification of a novel class of selective Tpl2 kinase inhibitors:

pp 6425–6442

#### 4-Alkylamino-[1,7]naphthyridine-3-carbonitriles

Neelu Kaila,\* Neal Green, Huan-Qiu Li, Yonghan Hu, Kristin Janz, Lori Krim Gavrin, Jennifer Thomason, Steve Tam, Dennis Powell, John Cuozzo, J. Perry Hall, Jean-Baptiste Telliez, Sang Hsu, Cheryl Nickerson-Nutter, Qin Wang and Lih-Ling Lin

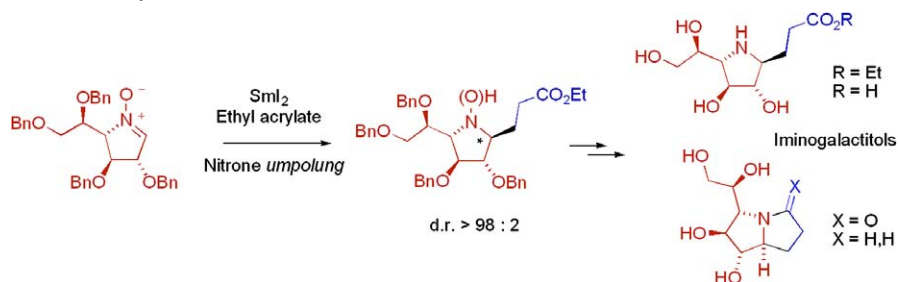
A series of 4-alkylamino-[1,7]naphthyridine-3-carbonitriles were synthesized and evaluated for activity against Tpl2 kinase. The 4-cycloheptylamino analog **30** demonstrated efficacy in a rat model of LPS-induced TNF- $\alpha$  production.



### Stereoselective synthesis of $\beta$ -1-C-substituted 1,4-dideoxy-1,4-imino-D-galactitols and evaluation as UDP-galactopyranose mutase inhibitors

pp 6443–6449

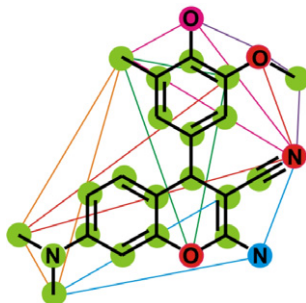
Stéphanie Desvergnès, Valérie Desvergnès,\* Olivier R. Martin, Kenji Itoh, Hung-wen Liu and Sandrine Py\*



### Novel TOPP descriptors in 3D-QSAR analysis of apoptosis inducing 4-aryl-4*H*-chromenes: Comparison versus other 2D- and 3D-descriptors

pp 6450–6462

Simone Sciabola,\* Emanuele Carosati, Lourdes Cucurull-Sanchez, Massimo Baroni and Raimund Mannhold\*



### Comparative molecular field analysis of flavonoid inhibitors of the PIM-1 kinase

pp 6463–6473

Sheldon Holder, Michael Lilly and Milton L. Brown\*

A predictive CoMFA model of flavonoid inhibitors of the PIM-1 kinase is reported. Shown is the alignment rule for the training set of compounds used to build the CoMFA model.

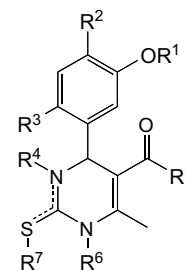


### New chemical tools for investigating human mitotic kinesin Eg5

pp 6474–6488

Emmanuel Klein, Salvatore DeBonis, Bernd Thiede, Dimitrios A. Skoufias, Frank Kozielski and Luc Lebeau\*

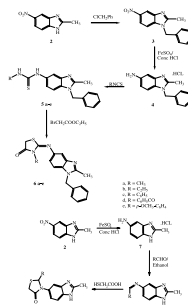
Monastrol is a specific allosteric inhibitor of Eg5, a kinesin responsible for the formation and maintenance of the bipolar spindle. In contrast to anticancer drugs that perturb mitosis and all target tubulin, it does not display any neurotoxicity and thus is thought to have antitumor potential. A series of analogs have been synthesized and tested for inhibition of Eg5 in vitro and for arresting mitosis of cultured cells. One compound was more potent than parent monastrol by a fivefold factor. Structure–activity relationships led to the preparation of an affinity matrix for unprecedentedly fast and efficient purification of full-length Eg5 from eukaryotic cells. The question of monastrol-targets other than Eg5 is discussed.



### Synthesis and inhibitory activity of new benzimidazole derivatives against Burkitt's lymphoma promotion


pp 6489–6496

Mostafa. M. Ramla,\* Mohamed. A. Omar, H. Tokuda and Hoda. I. El-Diwani



**OTHER CONTENTS****Summary of instructions to authors****p I**

\*Corresponding author

+ Supplementary data available via ScienceDirect**COVER**

Terfenadine (an antihistamine pulled from the market in 1997) bound to a model of an open form of the homo-tetrameric pore domain of hERG, produced using Schrödinger's "Induced Fit Docking" technology [Farid, R.; Day, T.; Friesner, R. A.; Pearlstein, R. A. *Bioorg. Med. Chem.* **2006**, *14*, 3160–3173].

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