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# Bioorganic & Medicinal Chemistry

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## Bioorganic & Medicinal Chemistry Volume 18, Issue 10, 2010

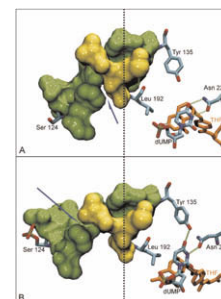
### Contents

#### ARTICLES

#### Mechanism of influence of phosphorylation on serine 124 on a decrease of catalytic activity of human thymidylate synthase pp 3361–3370

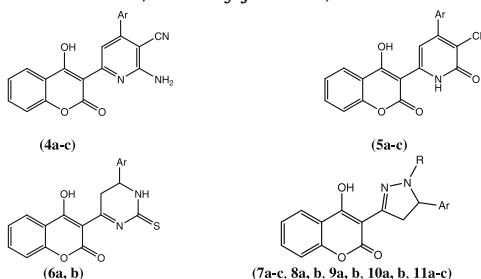
Adam Jarmuła\*, Tomasz Frączyk, Piotr Cieplak, Wojciech Rode

Molecular modeling studies aimed at the explanation of reduced catalytic activity of human thymidylate synthase phosphorylated on serine 124 are reported.



#### Synthesis, anticoagulant and PIVKA-II induced by new 4-hydroxycoumarin derivatives pp 3371–3378

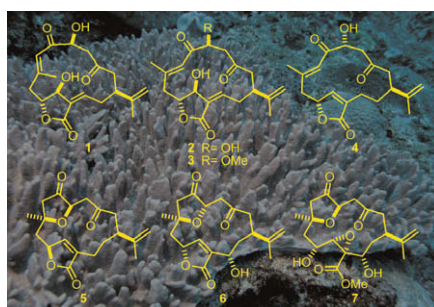
Omaima M. Abdelhafez\*, Kamelia M. Amin, Rasha Z. Batran, Timothy J. Maher, Somaia A. Nada, Shalini Sethumadhavan



3-Pyridinyl, pyrimidinyl and pyrazolyl-4-hydroxycoumarin derivatives were synthesized. A comparative in vivo (CT, PT determination) and in vitro (measurement of PIVKA-II levels) anticoagulant study with respect to warfarin showed that the synthesized compounds have different anticoagulant activities, the most prospective compounds were the 3-pyrazolyl-4-hydroxycoumarin derivatives.

#### Bioactive norditerpenoids from the soft coral *Sinularia gyrosa* pp 3379–3386

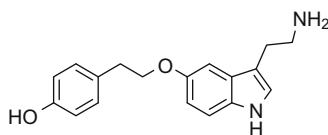
Shi-Yie Cheng, Cheng-Ta Chuang, Zhi-Hong Wen, Shang-Kwei Wang, Shu-Fen Chiou, Chi-Hsin Hsu, Chang-Feng Dai, Chang-Yih Duh\*



### Serotonin derivatives as a new class of non-ATP-competitive receptor tyrosine kinase inhibitors

pp 3387–3402

Anita Büttner, Thomas Cottin, Jing Xu, Lito Tzagkaroulaki, Athanassios Giannis\*

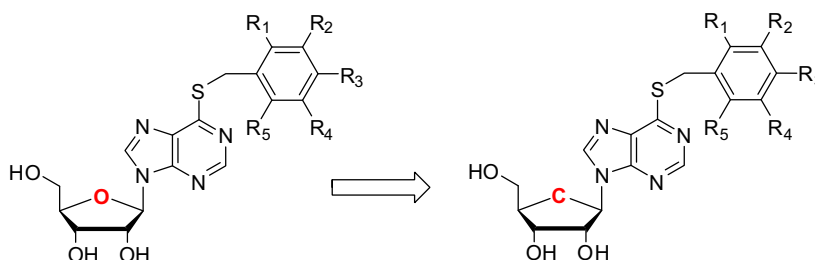


Herein we report the discovery of serotonin derivatives as a novel type of non-ATP-competitive RTK inhibitors.

### Structure–activity relationships of carbocyclic 6-benzylthioinosine analogues as subversive substrates of *Toxoplasma gondii* adenosine kinase

pp 3403–3412

Young Ah Kim, Ravindra K. Rawal, Jakyung Yoo, Ashoke Sharon, Ashok K. Jha, Chung K. Chu\*, Reem H. Rais, Omar N. Al Safarjalani, Fardos N. M. Naguib, Mahmoud H. el Kouni

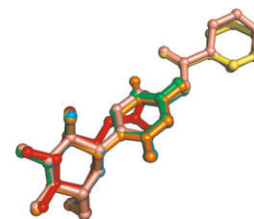


### 1-(3-Deoxy-3-fluoro-β-D-glucopyranosyl) pyrimidine derivatives as inhibitors of glycogen phosphorylase b: Kinetic, crystallographic and modelling studies

pp 3413–3425

Vicky G. Tsirkone, Evangelia Tsoukala, Christos Lamprakis, Stella Manta, Joseph M. Hayes, Vicky T. Skamnaki, Christina Drakou, Spyros E. Zographos, Dimitri Komiotis, Demetres D. Leonidas\*

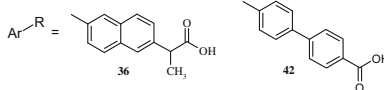
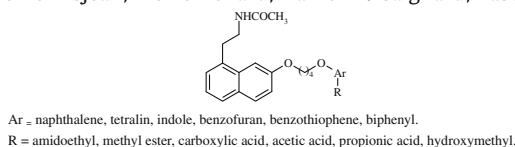
The catalytic site of muscle glycogen phosphorylase b (GPb) has been probed with five fluorine glucose derivatives. These inhibitors had fluorine instead of hydroxyl at the 3' position of the glucose moiety and a variety of pyrimidine derivatives at the 1' position. The best of this carbohydrate-based family of five inhibitors displays a  $K_i$  value of 46  $\mu\text{M}$ .



### Design, synthesis and pharmacological evaluation of novel naphthalenic derivatives as selective MT<sub>1</sub> melatonergic ligands

pp 3426–3436

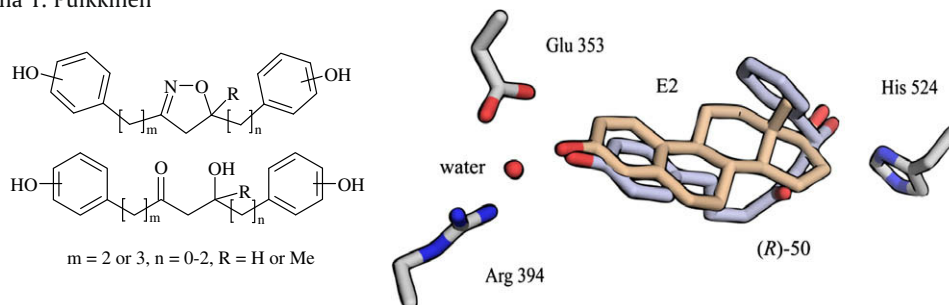
Christophe Mésangeau, Basile Pérès, Carole Descamps-François, Philippe Chavatte, Valérie Audinot, Sophie Coumailleau, Jean A. Boutin, Philippe Delagrangé, Caroline Bennejean, Pierre Renard, Daniel H. Caignard, Pascal Berthelot, Saïd Yous\*



### Synthesis and biological evaluation of phenolic 4,5-dihydroisoxazoles and 3-hydroxy ketones as estrogen receptor $\alpha$ and $\beta$ agonists

pp 3437–3447

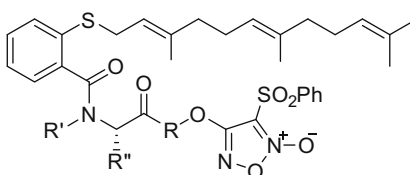
Pekka K. Poutiainen, Tuomas A. Venäläinen, Mikael Peräkylä, Juha M. Matilainen, Sami Väisänen, Paavo Honkakoski, Reino Laatikainen, Juha T. Pulkkinen\*



### Synthesis and evaluation of nitric oxide-releasing derivatives of farnesylthiosalicylic acid as anti-tumor agents

pp 3448–3456

Yong Ling, Xiaolei Ye, Hui Ji\*, Yihua Zhang\*, Yisheng Lai, Sixun Peng, Jide Tian

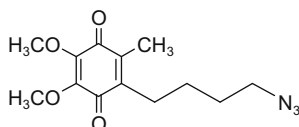


A series of novel furoxan-based nitric oxide (NO)-releasing derivatives of farnesylthiosalicylic acid (FTA) were synthesized and evaluated for their cytotoxicity against human cancer cells, NO-releasing ability and Ras inhibitory activity.

### Photolabile ubiquinone analogues for identification and characterization of quinone binding sites in proteins

pp 3457–3466

Zhichao Pei, Tobias Gustavsson, Robert Roth, Torbjörn Frejd, Cecilia Hägerhäll\*



Novel azidoquinone for direct photolabeling of quinone binding sites in proteins.

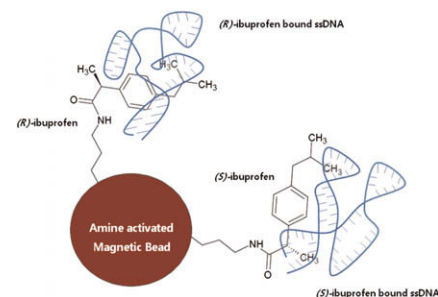


### Isolation and characterization of enantioselective DNA aptamers for ibuprofen

pp 3467–3473

Yeon Seok Kim, Chang Jun Hyun, In Ae Kim, Man Bock Gu\*

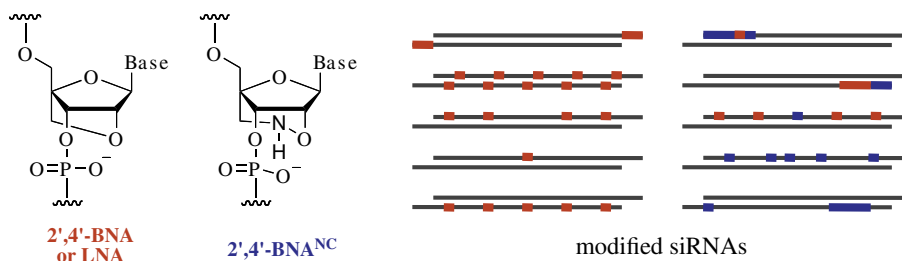
Racemic form of ibuprofen was immobilized on amine functionalized magnetic beads and enantioselective DNA aptamers were selected for (S)- and (R)-ibuprofen based on conformational interactions.



### RNA interference with 2',4'-bridged nucleic acid analogues

pp 3474–3480

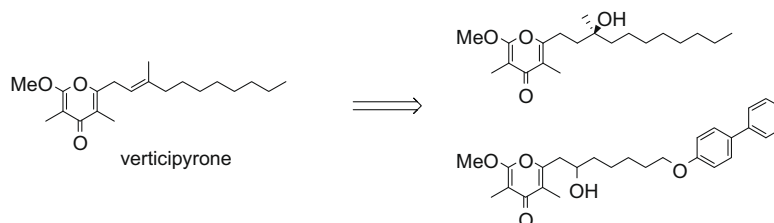
S. M. Abdur Rahman, Hiroyuki Sato, Naoto Tsuda, Sunao Haitani, Keisuke Narukawa, Takeshi Imanishi, Satoshi Obika\*



### Synthesis and evaluation of verticypyrone analogues as mitochondrial complex I inhibitors

pp 3481–3493

Simon J. Leiris, Omar M. Khdour, Zachary J. Segerman, Krystal S. Tsosie, Jean-Charles Chapuis, Sidney M. Hecht\*

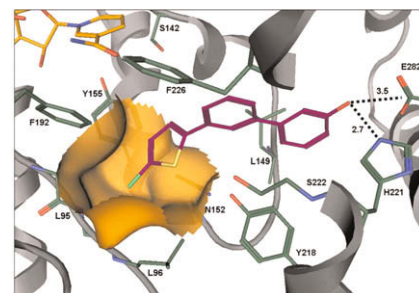
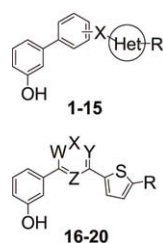


### Novel estrone mimetics with high 17 $\beta$ -HSD1 inhibitory activity

pp 3494–3505

Alexander Oster, Tobias Klein, Ruth Werth, Patricia Kruchten, Emmanuel Bey, Matthias Negri, Sandrine Marchais-Oberwinkler, Martin Frotscher, Rolf W. Hartmann\*

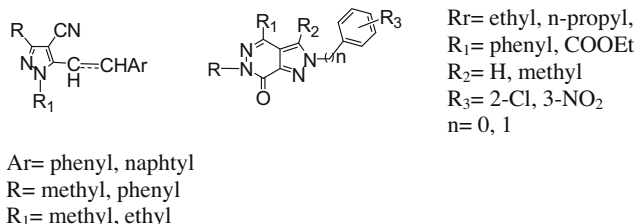
Estrone mimetics were synthesized and 17 $\beta$ -HSD1 inhibition was determined. Compound **12** showed high inhibitory activity, selectivity toward 17 $\beta$ -HSD2, ER $\alpha$ /ER $\beta$  and its binding mode shed light on a subpocket as interacting area.



### Functionalized pyrazoles and pyrazolo[3,4-d]pyridazinones: Synthesis and evaluation of their phosphodiesterase 4 inhibitory activity

pp 3506–3517

Pierfrancesco Biagini, Claudio Biancalani, Alessia Graziano, Nicoletta Cesari, Maria Paola Giovannoni\*, Agostino Cilibrizzi, Vittorio Dal Piaz, Claudia Vergelli, Letizia Crocetti, Maurizio Delcanale, Elisabetta Armani, Andrea Rizzi, Paola Puccini, Paola Maria Gallo, Daniele Spinabelli, Paola Caruso

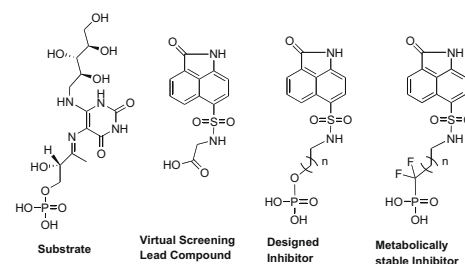


### Virtual screening, selection and development of a benzindolone structural scaffold for inhibition of lumazine synthase

pp 3518–3534

Arindam Talukdar, Ekaterina Morgunova, Jianxin Duan, Winfried Meining, Nicolas Foloppe, Lennart Nilsson, Adelbert Bacher, Boris Illarionov, Markus Fischer, Rudolf Ladenstein, Mark Cushman\*

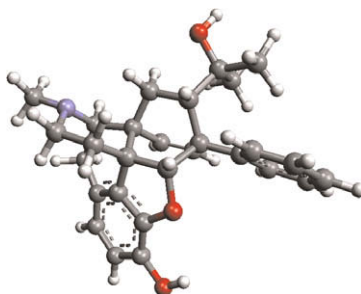
Virtual screening of compounds versus *Mycobacterium tuberculosis* lumazine synthase put forth a possible lead compound. Lead optimization through replacement of carboxymethylsulfonamide side chain led to compound that display modest enzyme inhibitory activity.



### Synthesis and opioid activity of novel 6-substituted-6-demethoxy-ethenomorphinans

pp 3535–3542

Barbara Czakó, János Marton, Sándor Berényi, Katarzyna Gach, Jakub Fichna, Martin Storr, Géza Tóth, Attila Sipos\*, Anna Janecka

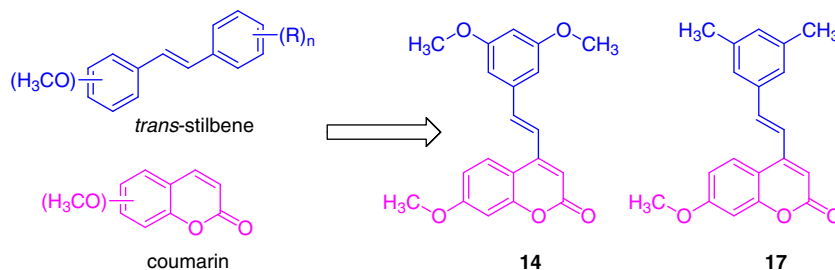


Nanomolar affinity to opioid receptors and antagonistic profile at the opioid receptors in the mouse ileum.

### Design, synthesis and anticancer activities of stilbene-coumarin hybrid compounds: Identification of novel proapoptotic agents

pp 3543–3550

Federica Belluti\*, Gabriele Fontana, Laura Dal Bo, Nives Carenini, Chiara Giommarelli, Franco Zunino

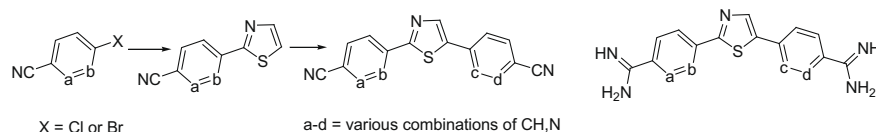


A series of novel stilbene-coumarin hybrid compounds were synthesized and evaluated for their antiproliferative and proapoptotic activities. The most promising compounds in this series were **14** and **17**, endowed with excellent antiproliferative and proapoptotic activities.

### Synthesis and antiprotozoal activity of 2,5-bis[amidinoaryl]thiazoles

pp 3551–3558

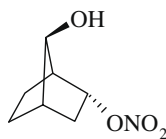
Danuta Branowska, Abdelbasset A. Farahat, Arvind Kumar, Tanja Wenzler, Reto Brun, Yang Liu, W. David Wilson, David W. Boykin\*



**NO-releasing esters show carbonic anhydrase inhibitory action against human isoforms I and II**

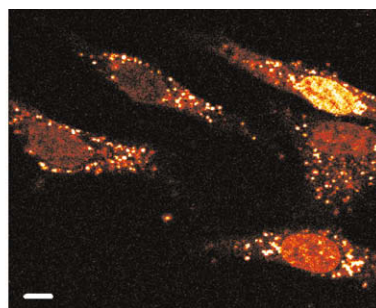
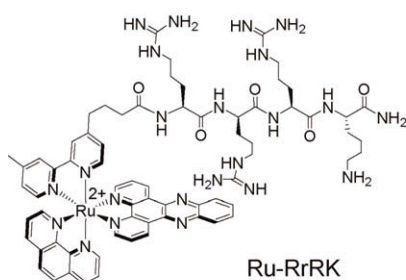
pp 3559–3563

Deniz Ekinci\*, Hüseyin Çavdar, Oktay Talaz, Murat Şentürk, Claudiu T. Supuran\*

 $I_{50} = 7.13 \text{ mM (hCA I)} ; I_{50} = 65.1 \text{ }\mu\text{M (hCA II)}$ **Targeting a ruthenium complex to the nucleus with short peptides**

pp 3564–3569

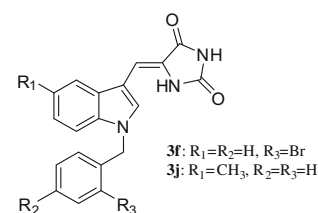
Cindy A. Puckett, Jacqueline K. Barton\*

**Aplysinopsin analogs: Synthesis and anti-proliferative activity of substituted (Z)-5-(N-benzylindol-3-ylmethylene)imidazolidine-2,4-diones**

pp 3570–3574

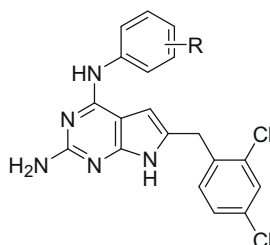
Y. Thirupathi Reddy, P. Narsimha Reddy, Srinivas Koduru, Chendil Damodaran, Peter A. Crooks\*

A series of substituted (Z)-5-(N-benzylindol-3-ylmethylene)imidazolidine-2,4-dione (**3**) analogs structurally related to aplysinopsin, and that incorporate a variety of substituents in both the indole and N-benzyl moieties have been synthesized under microwave irradiation and conventional heating methods. These analogs were evaluated for their anti-proliferative activity against MCF-7 and MDA-231 breast cancer cell lines, and A549 and H460 lung cancer cell lines. Two analogs, **3f** and **3j** had  $IC_{50}$  values of 4.4 and 5.2  $\mu\text{M}$ , respectively, compared to 5-fluorouracil ( $IC_{50} = 15.2 \text{ }\mu\text{M}$ ) against MCF-7 cells.

**Synthesis and biological activity of *N*<sup>4</sup>-phenylsubstituted-6-(2,4-dichloro phenylmethyl)-7*H*-pyrrolo[2,3-*d*]-pyrimidine-2,4-diamines as vascular endothelial growth factor receptor-2 inhibitors and antiangiogenic and antitumor agents**

pp 3575–3587

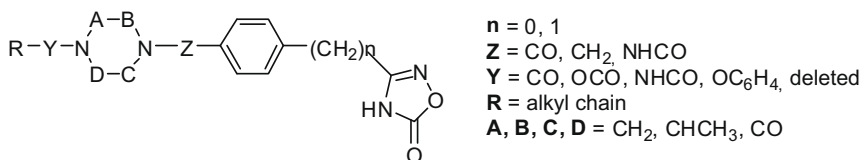
Aleem Gangjee\*, Sonali Kurup, Michael A Ihnat, Jessica E. Thorpe, Satyendra S. Shenoy



### Design of new potent and selective secretory phospholipase A<sub>2</sub> inhibitors. 6-Synthesis, structure–activity relationships and molecular modelling of 1-substituted-4-[4,5-dihydro-1,2,4-(4H)-oxadiazol-5-one-3-yl(methyl)]-functionalized aryl piperazin/one/dione derivatives

pp 3588–3600

Nadia Meddad-Belhabich, Darina Aoun, Atimé Djimdé, Catherine Redeuilh, Georges Dive, France Massicot, François Chau, Françoise Heymans, Aazdine Lamouri\*

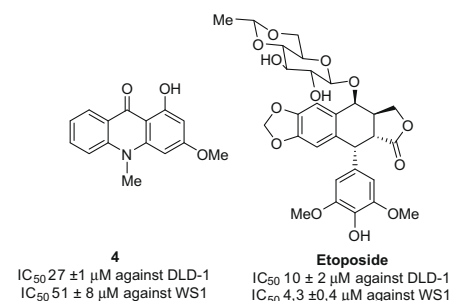


### In vitro cytotoxic activity of isolated acridones alkaloids from *Zanthoxylum lepreurii* Guill. et Perr

pp 3601–3605

Rostand M. Ngoumfo\*, Jean-Bosco Jouda, Ferdinand T. Mouafo, Justin Komguem, Céline D. Mbazona, Tze Chieh Shiao, Mohammed I. Choudhary, Hartmut Laatsch, Jean Legault, André Pichette, René Roy\*

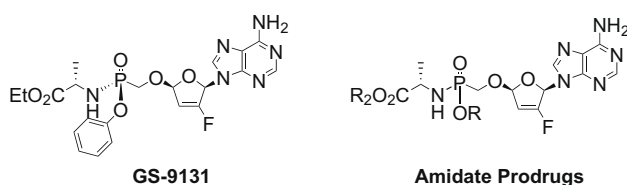
A family of acridones was isolated from *Zanthoxylum lepreurii* and their cytotoxicity was evaluated against lung carcinoma cells (A549), colorectal adenocarcinoma cells (DLD-1) and normal cells (WS1). In contrast to positive control etoposide, the cytotoxicity of the most active compound **4** was found to be selective against cancer cells in comparison to normal cells.



### Discovery of GS-9131: Design, synthesis and optimization of amidate prodrugs of the novel nucleoside phosphonate HIV reverse transcriptase (RT) inhibitor GS-9148

pp 3606–3617

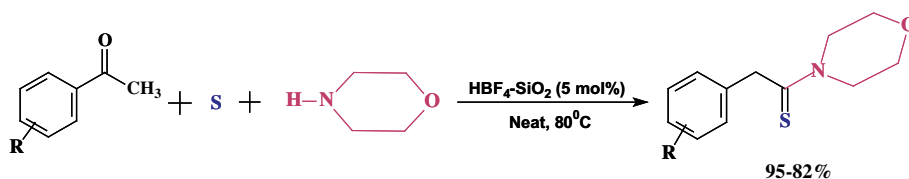
Richard L. Mackman\*, Adrian S. Ray, Hon C. Hui, Lijun Zhang, Gabriel Birkus, Constantine G. Booramra, Manoj C. Desai, Janet L. Douglas, Ying Gao, Deborah Grant, Genevieve Laflamme, Kuei-Ying Lin, David Y. Markevitch, Ruchika Mishra, Martin McDermott, Rowchanak Pakdaman, Oleg V. Petrakovsky, Jennifer E. Vela, Tomas Cihlar



### Silica-supported fluoroboric acid ( $\text{HBF}_4\text{-SiO}_2$ ) catalyzed highly productive synthesis of thiomorpholides as activators of L-asparaginase as well as the antioxidant agent

pp 3618–3624

Babasaheb P. Bandgar\*, Shrikant S. Gawande, Suchita C. Warangkar, Jalinder V. Totre




## OTHER CONTENT

## Corrigendum

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\*Corresponding author

 Supplementary data available via ScienceDirect

## COVER

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (<http://www.pymol.org>). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, 102, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, 61(6), 355–360].

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ISSN 0968-0896