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# Bioorganic & Medicinal Chemistry

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## Bioorganic & Medicinal Chemistry Volume 20, Issue 11, 2012

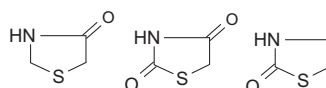
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#### REVIEW

##### Recent developments and biological activities of thiazolidinone derivatives: A review

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Abhishek Kumar Jain, Ankur Vaidya, Veerasamy Ravichandran, Sushil Kumar Kashaw, Ram Kishore Agrawal\*

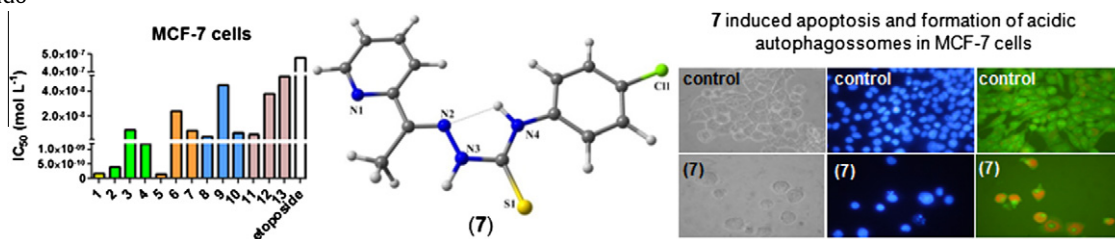


#### ARTICLES

##### N<sup>4</sup>-Phenyl-substituted 2-acetylpyridine thiosemicarbazones: Cytotoxicity against human tumor cells, structure–activity relationship studies and investigation on the mechanism of action

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Marcella A. Soares, Josane A. Lessa, Isolda C. Mendes, Jeferson G. Da Silva, Raquel G. dos Santos, Lívia B. Salum, Hikmat Daghestani, Adriano D. Andricopulo, Billy W. Day, Andreas Vogt, Jorge L. Pesquero, Willian R. Rocha, Heloisa Beraldo\*

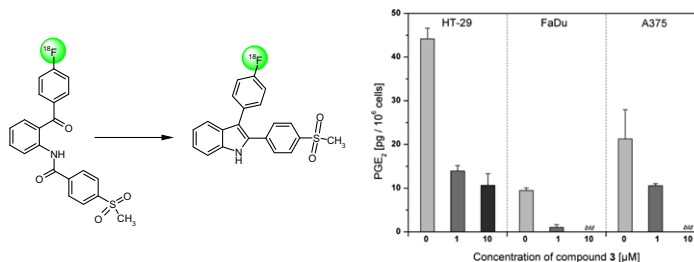


##### Radiosynthesis of a <sup>18</sup>F-labeled 2,3-diarylsubstituted indole via McMurry coupling for functional characterization of cyclooxygenase-2 (COX-2) in vitro and in vivo

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Torsten Kniess\*, Markus Laube, Ralf Bergmann, Fabian Sehn, Franziska Graf, Joerg Steinbach, Frank Wuest, Jens Pietzsch

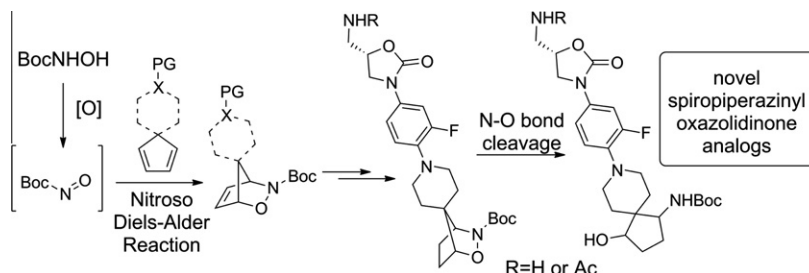
The radiosynthesis of a 2,3-diarylsubstituted indole via McMurry cyclization as potential PET probe for functional characterization of cyclooxygenase-2 (COX-2) is described. The radiotracer was evaluated in vitro using COX-2 expressing tumor cell lines and in vivo by dynamic small animal PET studies on HT-29 tumor-bearing mice.



### Syntheses and biological studies of novel spiropiperazinyl oxazolidinone antibacterial agents using a spirocyclic diene derived acylnitroso Diels–Alder reaction

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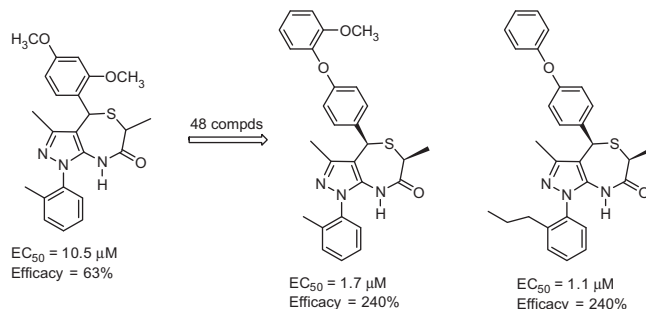
Cheng Ji, Weimin Lin, Garrett C. Moraski, Jane A. Thanassi, Michael J. Pucci, Scott G. Franzblau, Ute Möllmann, Marvin J. Miller\*



### Pyrazole[3,4-e][1,4]thiazepin-7-one derivatives as a novel class of Farnesoid X Receptor (FXR) agonists

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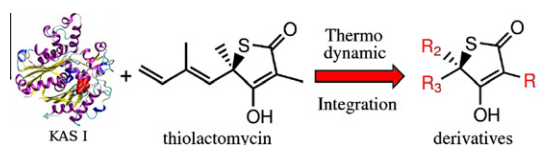
Maura Marinozzi\*, Andrea Carotti, Emanuele Sansone, Antonio Macchiarulo, Emiliano Rosatelli, Roccaldo Sardella, Benedetto Natalini, Giovanni Rizzo, Luciano Adorini, Daniela Passeri, Francesca De Franco, Mark Pruzanski, Roberto Pellicciari



### Free energy calculations on the binding of novel thiolactomycin derivatives to *E. coli* fatty acid synthase I

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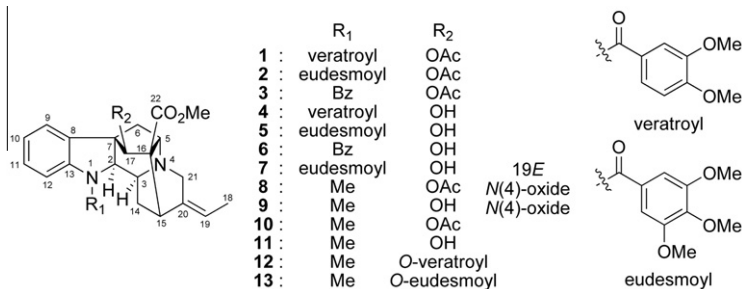
Thomas Steinbrecher\*, David A. Case, Andreas Labahn



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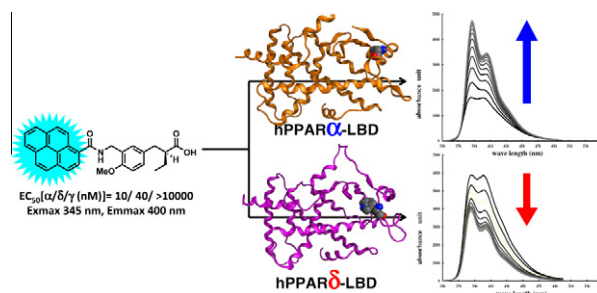
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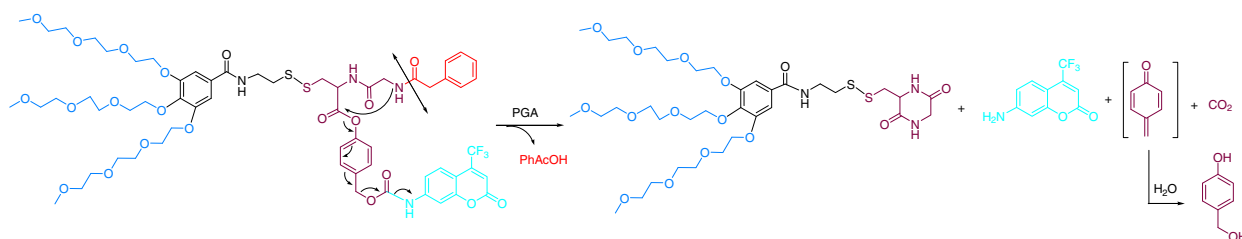
**Bidirectional fluorescence properties of pyrene-based peroxisome proliferator-activated receptor (PPAR)  $\alpha/\delta$  dual agonist**

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Shintaro Ban, Takuji Oyama, Jun-ichi Kasuga, Kenji Ohgane, Yoshino Nishio, Kosuke Morikawa, Yuichi Hashimoto, Hiroyuki Miyachi\*

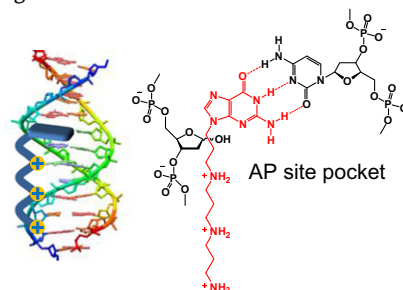
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**Synthesis and binding properties of new selective ligands for the nucleobase opposite the AP site**

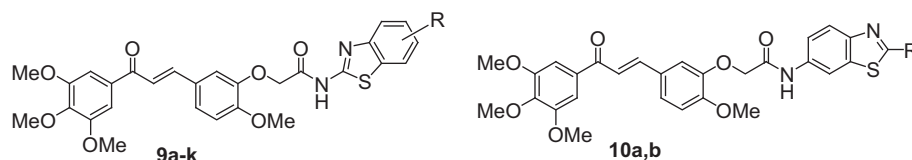
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**Synthesis of chalcone-amidobenzothiazole conjugates as antimitotic and apoptotic inducing agents**

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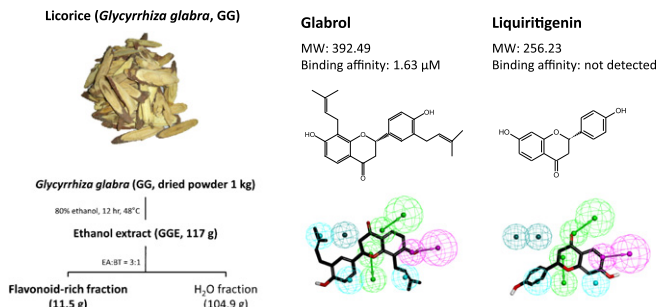
Ahmed Kamal\*, Adla Mallareddy, Paidakula Suresh, Thokhir B. Shaik, V. Lakshma Nayak, Chandan Kishor, Rajesh V.C.R.N.C. Shetti, N. Sankara Rao, Jaki R. Tamboli, S. Ramakrishna, Anthony Addlagatta\*



## Hypnotic effects and GABAergic mechanism of licorice (*Glycyrrhiza glabra*) ethanol extract and its major flavonoid constituent glabrol pp 3493–3501

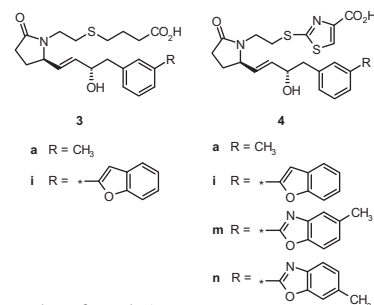
Suengmok Cho, Ji-Hae Park, Ae Nim Pae, Daeseok Han, Dongsoo Kim, Nam-Chul Cho, Kyoung Tai No, Hyejin Yang, Minseok Yoon, Changho Lee, Makoto Shimizu\*, Nam-In Baek\*

Licorice ethanol extract and its flavonoid-rich fraction and glabrol induce sleep via a positive allosteric modulation of GABA<sub>A</sub>-BZD receptors. The binding affinity and pharmacophore model of glabrol and liquiritigenin indicate that the isoprenyl groups of glabrol may play a key role in binding to GABA<sub>A</sub>-BZD receptors.



## Synthesis and evaluation of $\gamma$ -lactam analogs of PGE<sub>2</sub> as EP4 and EP2/EP4 agonists pp 3502–3522

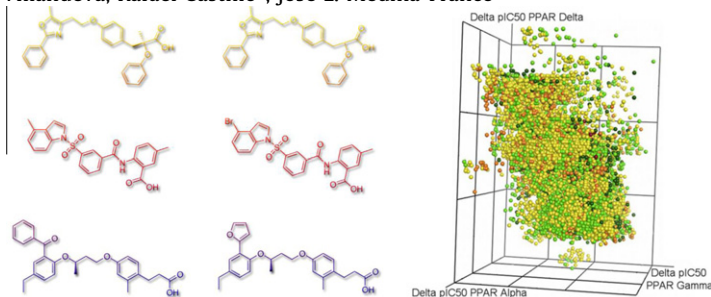
Tohru Kambe\*, Toru Maruyama, Yoshihiko Nakai, Hiroji Oida, Takayuki Maruyama, Nobutaka Abe, Akio Nishiura, Hisao Nakai, Masaaki Toda



EP4 subtype-selective agonists **3** and EP2/EP4 dual agonists **4** were optimized for their sustained release from PLGA microsphere formulation.

## Activity landscape modeling of PPAR ligands with dual-activity difference maps pp 3523–3532

Oscar Méndez-Lucio, Jaime Pérez-Villanueva, Rafael Castillo\*, José L. Medina-Franco\*

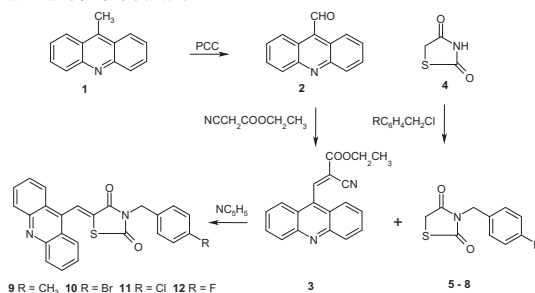


A systematic characterization of the structure–activity relationships of diverse compounds with reported activity against PPAR $\alpha$ , PPAR $\delta$ , and PPAR $\gamma$ .



## Synthesis and cytotoxic activity of new acridine-thiazolidine derivatives pp 3533–3539

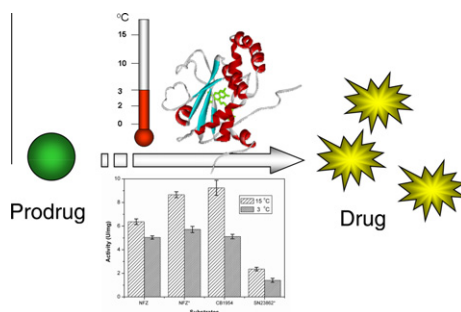
Francisco W. A. Barros, Teresinha Gonçalves Silva, Marina Galdino da Rocha Pitta, Daniel P. Bezerra, Letícia V. Costa-Lotufo, Manoel Odorico de Moraes, Cláudia Pessoa, Maria Aline F. B. de Moura, Fabiane C. de Abreu, Maria do Carmo Alves de Lima, Suely Lins Galdino, Ivan da Rocha Pitta\*, Marília O. F. Goulart\*



**An unusually cold active nitroreductase for prodrug activations**

pp 3540–3550

Ayhan Çelik\*, Gülden Yetiş

**Synthesis, anticonvulsant activity, and neuropathic pain-attenuating activity of *N*-benzyl 2-amino-2-(hetero)aromatic acetamides**

pp 3551–3564

Pranjal K. Baruah, Jason Dinsmore, Amber M. King, Christophe Salomé, Marc De Ryck, Rafal Kaminski, Laurent Provins, Harold Kohn\*

CC(=O)Nc1ccccc1  
**FAA**  
 Ar = aromatic, heteroaromatic

CC(=O)Nc1ccccc1  
**PAAD**  
 Ar = aromatic, heteroaromatic

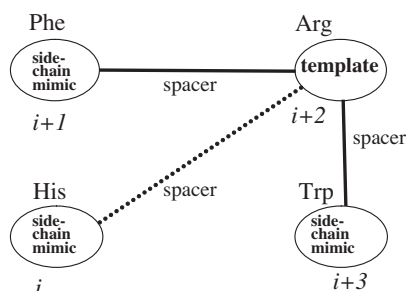
| Ar | FAA<br>MES<br>ED <sub>50</sub> (mg/kg) | PAAD<br>MES<br>ED <sub>50</sub> (mg/kg) | PAAD<br>Formalin<br>ED <sub>50</sub> (mg/kg) |
|----|----------------------------------------|-----------------------------------------|----------------------------------------------|
|    | 11                                     | 100<br>(MAD) <sup>a</sup>               | 33                                           |
|    | 15                                     | 85                                      | >160                                         |
|    | 10                                     | 85                                      | 29                                           |
|    | 12                                     | 67                                      | 45                                           |

<sup>a</sup>MAD = minimal active dose

**Automated generation of turn mimetics: Proof of concept study for the MC4 receptor**

pp 3565–3574

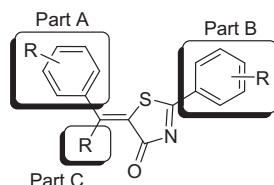
J. Christian Baber, Richard Lowe, John Saunders, Miklos Feher\*

**Synthesis and biological evaluation of a class of 5-benzylidene-2-phenyl-thiazolinones as potent 5-lipoxygenase inhibitors**

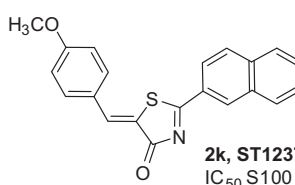
pp 3575–3583

Sebastian Barzen, Carmen B. Rödl, Andreas Lill, Dieter Steinhilber, Holger Stark\*, Bettina Hofmann\*

General structure:



Most active compound:



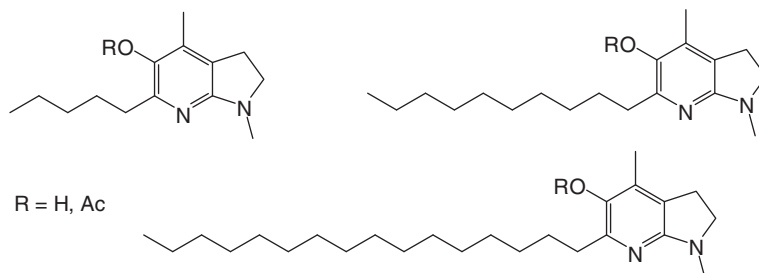
**2k, ST1237**  
 IC<sub>50</sub> S100 = 0.08 μM  
 IC<sub>50</sub> PMNL = 0.12 μM



### Simplified bicyclic pyridinol analogues protect mitochondrial function

pp 3584–3595

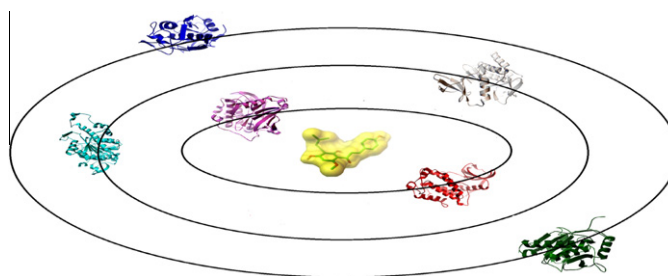
Xiaoqing Cai, Omar M. Khmour, Jennifer Jaruvangsanti, Sidney M. Hecht\*



### Inverse Virtual Screening allows the discovery of the biological activity of natural compounds

pp 3596–3602

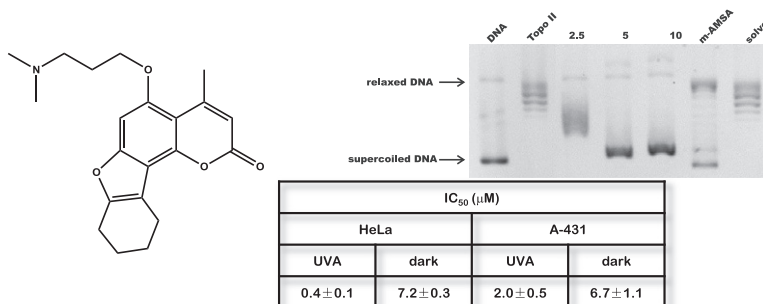
Gianluigi Lauro, Milena Masullo, Sonia Piacente, Raffaele Riccio, Giuseppe Bifulco\*



### A novel tetrahydrobenzoangelicin with dark and photo biological activity

pp 3603–3608

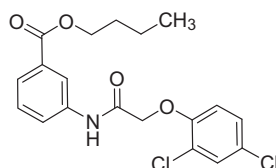
Lisa Dalla Via\*, Ornella Gia, Sergio Caffieri, Aída N. García-Argáez, Elías Quezada, Eugenio Uriarte



### Novel inhibitors of heat shock protein Hsp70-mediated luciferase refolding that bind to DnaJ

pp 3609–3614

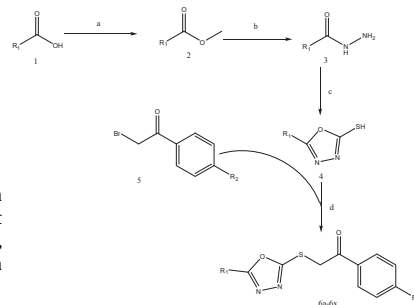
Joel A. Cassel\*, Sergey Ilyin, Mark E. McDonnell, Allen B. Reitz



Compound **6**, butyl 3-[2-(2,4-dichlorophenoxy)acetamido]benzoate, binds to DnaJ and inhibits Hsp70/DnaJ protein refolding with an IC<sub>50</sub> value of 0.13 μM.

## Synthesis, biological evaluation and molecular docking studies of novel 2-(1,3,4-oxadiazol-2-ylthio)-1-phenylethanone derivatives pp 3615–3621

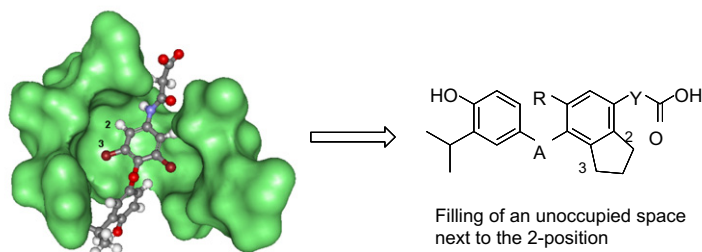
Li-Rong Zhang, Zhi-Jun Liu, Hui Zhang, Jian Sun, Yin Luo, Ting-Ting Zhao, Hai-Bin Gong\*, Hai-Liang Zhu\*



A series of new 2-(1,3,4-oxadiazol-2-ylthio)-1-phenylethanone derivatives (**6a–6x**) as potential focal adhesion kinase (FAK) inhibitors were synthesized. The bioassay tests demonstrated that compound **6i** showed the most potent activity, which inhibited the growth of MCF-7 and A431 cell lines with  $IC_{50}$  values of 0.14 and 0.01  $\mu$ M, respectively. Compound **6i** also exhibited significant FAK inhibitory activity ( $IC_{50}$  = 0.02  $\mu$ M). Docking simulation was performed to position compound **6i** into the active site of FAK to determine the probable binding model.

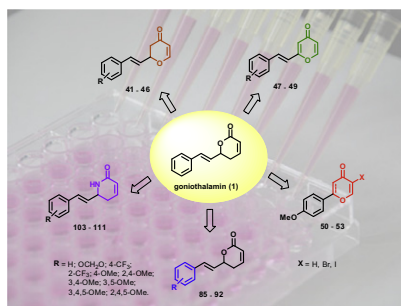
## Discovery of novel indane derivatives as liver-selective thyroid hormone receptor $\beta$ (TR $\beta$ ) agonists for the treatment of dyslipidemia pp 3622–3634

Hiroaki Shiohara\*, Tetsuya Nakamura, Norihiko Kikuchi, Tomonaga Ozawa, Ryuichi Nagano, Akane Matsuzawa, Hideki Ohnata, Takahide Miyamoto, Kazuo Ichikawa, Kiyoshi Hashizume



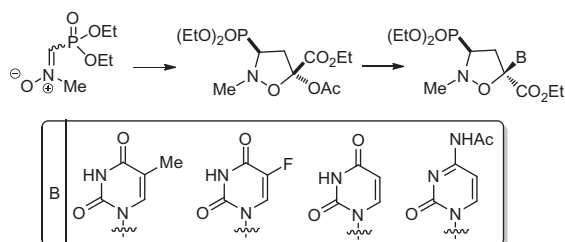
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Rosimeire Coura Barcelos, Julio Cezar Pastre, Vanessa Caixeta, Débora Barbosa Vendramini-Costa, João Ernesto de Carvalho, Ronaldo Aloise Pilli\*



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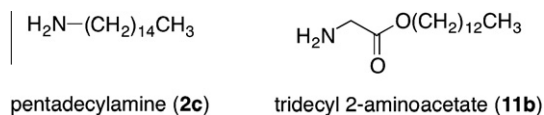
Roberto Romeo\*, Caterina Carnovale, Salvatore V. Giofrè, Giovanni Romeo, Beatrice Macchi, Caterina Frezza, Francesca Marino-Merlo, Venerando Pistarà, Ugo Chiacchio



**Lipophilic amines as potent inhibitors of *N*-acylethanolamine-hydrolyzing acid amidase**

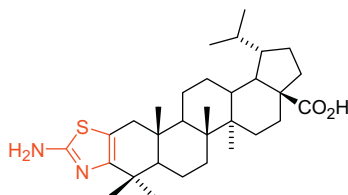
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Yumiko Yamano\*, Kazuhito Tsuboi, Yuki Hozaki, Kiyohiro Takahashi, Xing-Hua Jin, Natsuo Ueda, Akimori Wada

**Cytotoxic heterocyclic triterpenoids derived from betulin and betulinic acid**

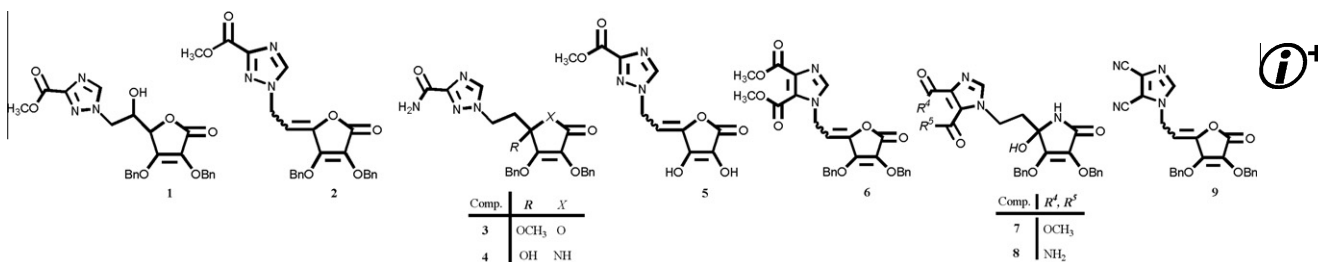
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Milan Urban, Martin Vlč, Petr Dzubak, Marian Hajduch, Jan Sarek\*

**Novel 1,2,4-triazole and imidazole derivatives of L-ascorbic and imino-ascorbic acid: Synthesis, anti-HCV and antitumor activity evaluations**

pp 3675–3685

Karlo Wittine, Maja Stipković Babić, Damjan Makuc, Janez Plavec, Sandra Kraljević Pavelić, Mirela Sedić, Krešimir Pavelić, Pieter Leyssen, Johan Neyts, Jan Balzarini, Mladen Mintas\*



\*Corresponding author

+ Supplementary data available via SciVerse ScienceDirect

## COVER

Dipyrone (metamizol) is a common antipyretic drug and the most popular non-opioid analgesic in many countries. In spite of its long and widespread use, molecular details of its fate in the body are not fully known. Two unknown metabolites were now found, viz. arachidonoyl amides, and positively tested for cannabis receptor binding (CB1 and CB2) and cyclooxygenase inhibition. Two more puzzle pieces of the dipyrone story found! (Rogosch, T.; Sinning, C.; Podlewski, A.; Watzer, B.; Schlosburg, J.; Lichtman, A.H.; Cascio, M.G.; Bisogno, T.; Di Marzo, V.; Nüsing, R.; Imming, P. *Bioorg. Med. Chem.* **2012**, 20, 103–109.)

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