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# Bioorganic & Medicinal Chemistry

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## Bioorganic & Medicinal Chemistry Volume 20, Issue 16, 2012

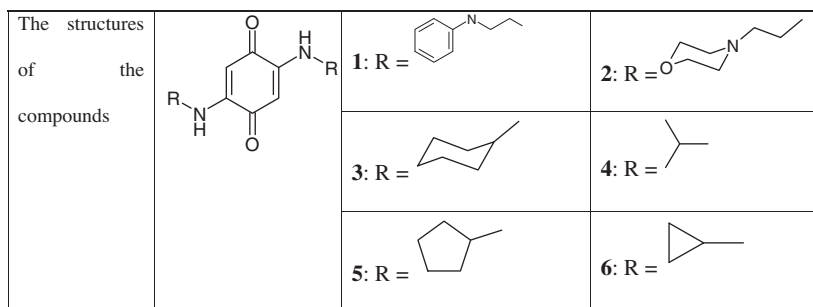
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#### Synthesis, biological evaluation, and molecular docking studies of 2,5-substituted-1,4-benzoquinone as novel urease inhibitors pp 4889–4894

Zhong-Lu You\*, Dong-Mei Xian,  
Mei Zhang, Xiao-Shan Cheng, Xiao-Fang Li

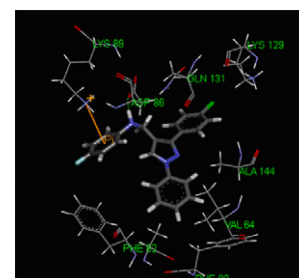
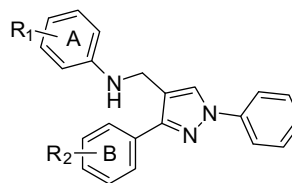
A series of 2,5-substituted-1,4-benzoquinone were prepared. The urease inhibitory activities and the molecular docking studies of the compounds against *Helicobacter pylori* urease were carried out. Three compounds bearing effective activities.



#### Synthesis, biological evaluation, and molecular docking studies of *N*-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyl)aniline derivatives as novel anticancer agents pp 4895–4900

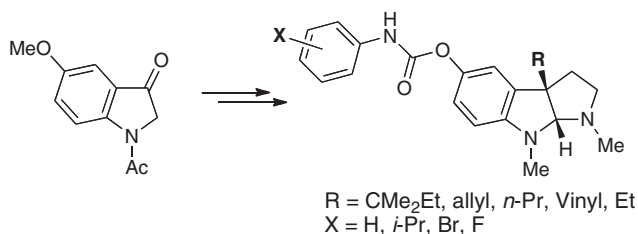
Xian-Feng Huang, Xiang Lu, Yong Zhang, Guo-Qiang Song, Qi-Long He, Qing-Shan Li, Xian-Hui Yang,  
Yao Wei, Hai-Liang Zhu\*

A series of novel *N*-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyl)aniline derivatives (**5a–8d**) have been designed and synthesized and evaluated as potential antitumor and cyclin dependent kinase 2 (CDK2) inhibitors. Among all the compounds, compound **5a** displayed the most potent CDK2/cyclin E inhibitory activity in vitro, with an  $IC_{50}$  of  $0.98 \pm 0.06 \mu M$ . Compound **5a** also owned high antiproliferative activity against MCF-7 and B16-F10 cancer cell lines with  $IC_{50}$  values of  $1.88 \pm 0.11$  and  $2.12 \pm 0.15 \mu M$ , respectively.



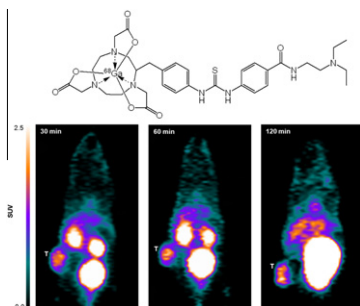
#### Synthesis of phenserine analogues and evaluation of their cholinesterase inhibitory activities pp 4901–4914

Masashi Shinada, Fuminori Narumi, Yuji Osada, Koji Matsumoto, Takayasu Yoshida, Kazuhiro Higuchi, Tomomi Kawasaki\*,  
Hiroyuki Tanaka, Mitsutoshi Satoh



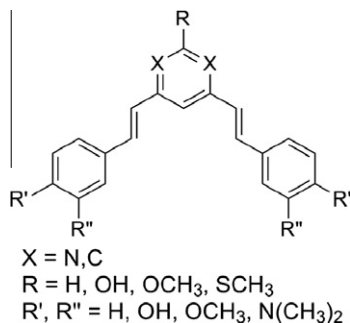
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Hee-Jung Kim, Dong-Yeon Kim, Jeong-Hoon Park, Seung-Dae Yang, Min-Goo Hur, Jung-Joon Min, Kook-Hyun Yu\*



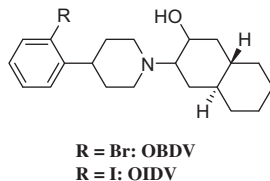
### Small molecules that protect against $\beta$ -amyloid-induced cytotoxicity by inhibiting aggregation of $\beta$ -amyloid pp 4921–4935

Yun Suk Lee, Hye Yun Kim, YoungSoo Kim, Jae Hong Seo, Eun Joo Roh, Hogyu Han, Kye Jung Shin\*



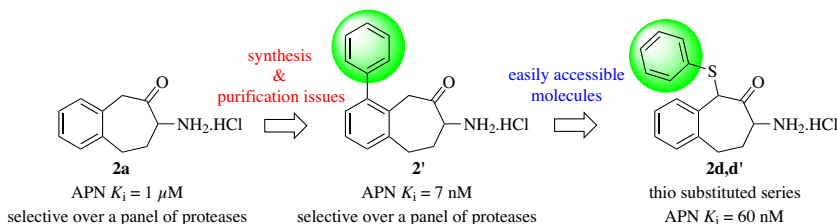
### Syntheses and in vitro evaluation of decalinvesamicol analogues as potential imaging probes for vesicular acetylcholine transporter (VAChT) pp 4936–4941

Takashi Kozaka\*, Izumi Uno, Yoji Kitamura, Daisuke Miwa, Kazuma Ogawa, Kazuhiro Shiba



### Rapid and efficient synthesis of a novel series of substituted aminobenzosuberone derivatives as potent, selective, non-peptidic neutral aminopeptidase inhibitors pp 4942–4953

Sébastien Albrecht\*, Emmanuel Salomon, Albert Defoin, Céline Tarnus\*



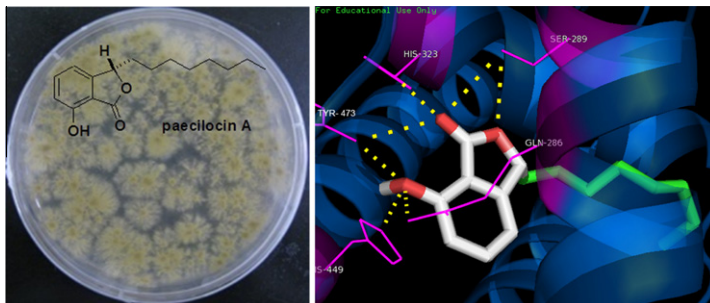
Some racemic aminobenzosuberone **2b–h** were readily synthesized and evaluated as inhibitors of a panel of zinc-dependent aminopeptidases.  $K_i$  values in the nanomolar range were obtained selectively against the one zinc aminopeptidase APN/CD13. The phenylthioether derivative **2d,d'** is among the most potent newly synthesized APN inhibitor and may exhibit a new type of binding mode.

**Design and synthesis of marine fungal phthalide derivatives as PPAR- $\gamma$  agonists**

pp 4954–4961

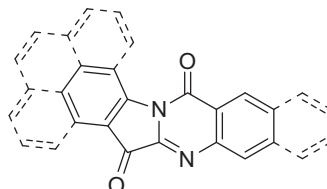
Bin Xiao, Jun Yin, Minhi Park, Juan Liu, Jian Lin Li, Eun La Kim, Jongki Hong, Hae Young Chung, Jee H. Jung\*

On the basis of a marine fungal phthalide (paecilocolin A) skeleton, we synthesized 20 analogs and evaluated them for peroxisome proliferator-activated receptor gamma (PPAR- $\gamma$ ) binding and activation. Among these analogs, **6** and **7** had significant PPAR- $\gamma$  binding activity, and **7** showed further PPAR- $\gamma$  activation in rat liver Ac2F cells. In docking simulation, **7** formed H bonds with key PPAR- $\gamma$ -binding domain amino acid residues, and the overall positioning was similar to rosiglitazone. This new phthalide derivative is considered an interesting new molecular class of PPAR- $\gamma$  ligands.

**Synthesis of benzo-annulated tryptanthrins and their biological properties**

pp 4962–4967

Jing Lu Liang, So-Eun Park, Youngjoo Kwon, Yurngdong Jahng\*

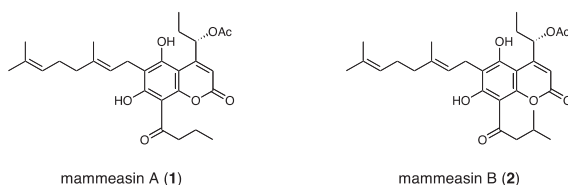


A series of benzo-annulated tryptanthrins were prepared and their physicochemical and biological properties were evaluated. Tryptanthrin and its benzo-annulated derivatives showed selective inhibitory activity on topo I with significant cytotoxicity against selected human cancer cell lines.

**Suppressive effects of coumarins from *Mammea siamensis* on inducible nitric oxide synthase expression in RAW264.7 cells**

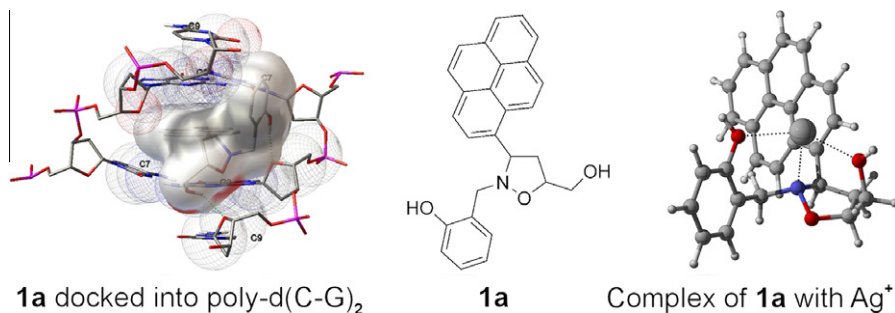
pp 4968–4977

Toshio Morikawa, Mayumi Sueyoshi, Saowanee Chaipetch, Hisashi Matsuda, Yukiko Nomura, Mikuko Yabe, Tomoko Matsumoto, Kiyofumi Ninomiya, Masayuki Yoshikawa, Yutana Pongpiriyadacha, Takao Hayakawa, Osamu Muraoka\*

**Synthesis and biological activity of novel bifunctional isoxazolidinyl polycyclic aromatic hydrocarbons**

pp 4978–4984

Antonio Rescifina\*, Chiara Zagni, Giovanni Romeo, Salvatore Sortino\*

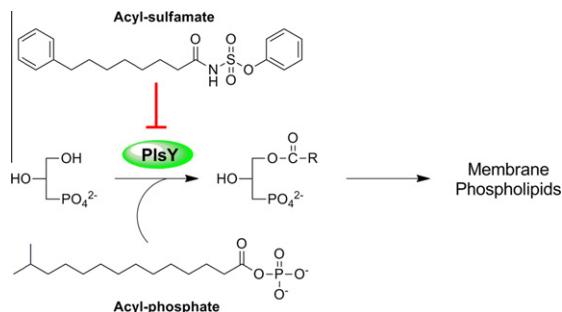


**Acyl-sulfamates target the essential glycerol-phosphate acyltransferase (PlsY) in Gram-positive bacteria**

pp 4985–4994

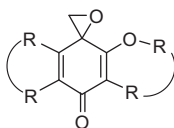
Philip T. Cherian, Jiangwei Yao, Roberta Leonardi, Marcus M. Maddox, Vicki A. Luna, Charles O. Rock, Richard E. Lee\*

A series of non-metabolizable, acyl-sulfamate analogs of the acyl-phosphate PlsY substrate were prepared and evaluated as inhibitors of *Staphylococcus aureus* PlsY and for their Gram-positive antibacterial activities.

**New oxirane derivatives of 1,4-naphthoquinones and their evaluation against *T. cruzi* epimastigote forms**

pp 4995–5000

Paula F. Carneiro, Samara B. do Nascimento, Antonio V. Pinto, Maria do Carmo F. R. Pinto, Guilherme C. Lechuga, Dilvani O. Santos, Helvécio M. dos Santos Júnior, Jackson A. L. C. Resende, Saulo C. Bourguignon\*, Vitor F. Ferreira\*

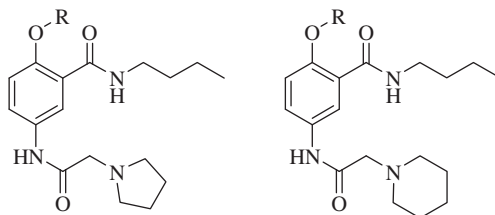


New oxirane derivatives were synthesized using six naphthoquinones as the starting material. Our biological results showed that these oxiranes acted as trypanocidal agents against *Trypanosoma cruzi* with minimal cytotoxicity in the VERO cell line compared to naphthoquinones. In particular, oxirane derivative **14** showed low cytotoxicity in a mammalian cell line and exhibited better activity against epimastigote forms of *T. cruzi* than the current drug used to treat Chagas disease, benznidazole.

**Synthesis of benzamide derivatives and their evaluation as antiprion agents**

pp 5001–5011

Ferdinando Fiorino, Martin Eiden, Armin Giese, Beatrice Severino, Antonella Esposito, Martin H. Groschup, Elisa Perissutti, Elisa Magli, Giuseppina Maria Incisivo, Antonio Ciano, Francesco Frecentese, Hans A. Kretzschmar, Jens Wagner, Vincenzo Santagada, Giuseppe Caliendo\*

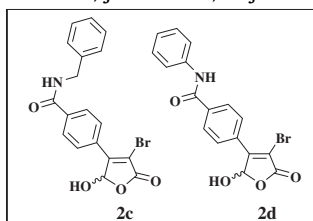


A new set of benzamide derivatives were synthesized in which as structural features the 2-(1-pyrrolidinyl)- or 2-(1-piperidyl)acetamino group or a diphenylether moiety are associated to a benzamide scaffold. Their binding affinity for human PrP<sup>C</sup> and inhibition of its conversion into PrP<sup>Sc</sup> were determined in vitro; moreover, the antiprion activity was assayed by inhibition of PrP<sup>Sc</sup> accumulation in scrapie-infected mouse neuroblastoma cells (ScN2a) and scrapie mouse brain (SMB) cells.

**Identification of new  $\gamma$ -hydroxybutenolides that preferentially inhibit the activity of mPGES-1**

pp 5012–5016

Rosa De Simone, Ines Bruno\*, Raffaele Riccio, Katharina Stadler, Julia Bauer, Anja M. Schaible, Stefan Laufer, Oliver Werz



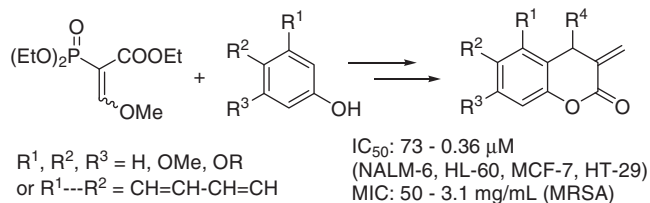
Microsomal prostaglandin E<sub>2</sub> synthase-1 (mPGES-1) is the terminal enzyme involved in the synthesis of the inducible prostaglandin E<sub>2</sub> in response to pro-inflammatory stimuli. It represents an extremely interesting target-enzyme for the development of safer anti-inflammatory drugs devoid of severe side effects typical for traditional drugs. In the course of our investigations focused on this topic, we identified two very interesting  $\gamma$ -hydroxybutenolide derivatives able to efficiently inhibit the catalytic activity of mPGES-1. Specifically, we discovered compound **2d** that inhibited mPGES-1 with IC<sub>50</sub> = 5.6  $\mu$ M and, above all, compound **2c** that inhibited the target-enzyme with IC<sub>50</sub> = 0.9  $\mu$ M without affecting other related enzymes within the arachidonic acid cascade.



**Synthesis and biological evaluation of  $\alpha$ -methylidene- $\delta$ -lactones with 3,4-dihydrocoumarin skeleton**

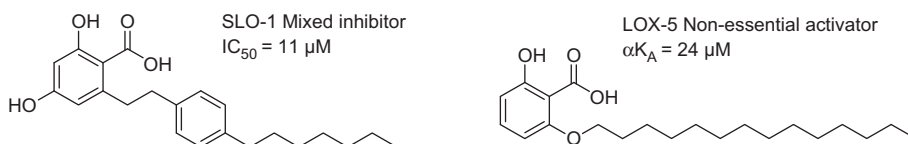
pp 5017–5026

Jakub Modranka, Anna Albrecht, Rafał Jakubowski, Henryk Krawczyk, Marek Różalski, Urszula Krajewska, Anna Janecka, Anna Wyrębska, Barbara Różalska, Tomasz Janecki\*

**Anacardic acid derived salicylates are inhibitors or activators of lipoxygenases**

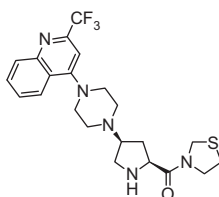
pp 5027–5032

Rosalina Wisastra, Massimo Ghizzoni, André Boltjes, Hidde J. Haisma, Frank J. Dekker\*

**Fused bicyclic heteroaryl piperazine-substituted L-prolylthiazolidines as highly potent DPP-4 inhibitors lacking the electrophilic nitrile group**

pp 5033–5041

Tomohiro Yoshida, Fumihiko Akahoshi\*, Hiroshi Sakashita, Shuji Sonda, Masahiro Takeuchi, Yoshihito Tanaka, Mika Nabeno, Hiroyuki Kishida, Ikuko Miyaguchi, Yoshiharu Hayashi



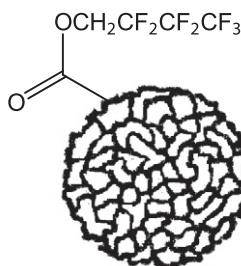
**8g**,  $\text{IC}_{50} = 0.37 \text{ nmol/L}$

A series of prolylthiazolidines with fused bicyclic heteroaryl piperazine substitution has been discovered as superior DPP-4 inhibitors, and the most potent **8g** showed high selectivity and in vivo efficacy.

**Attenuating the size and molecular carrier capabilities of polyacrylate nanoparticles by a hydrophobic fluorine effect**

pp 5042–5045

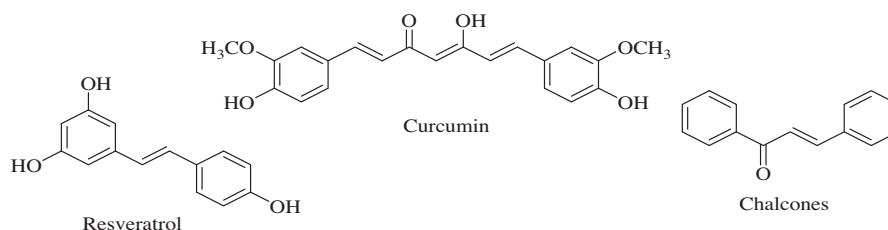
Raphaël Labruère, Edward Turos\*



**Effects of polyphenol compounds on influenza A virus replication and definition of their mechanism of action**

pp 5046–5052

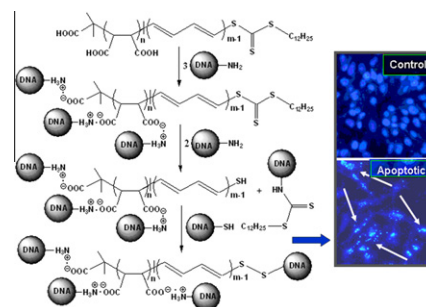
Rossella Fioravanti, Ignacio Celestino, Roberta Costi\*, Giuliana Cuzzucoli Crucitti, Luca Pescatori, Leonardo Mattiello, Ettore Novellino, Paola Checconi, Anna Teresa Palamara, Lucia Nencioni, Roberto Di Santo

**Bioengineering functional copolymers. XXI. Synthesis of a novel end carboxyl-trithiocarbonate functionalized poly(maleic anhydride) and its interaction with cancer cells**

pp 5053–5061

Zakir M. O. Rzayev\*, Mustafa Türk, Ernur A. Söylemez

Novel carboxyl-trithiocarbonate functionalized polymer with super selective antitumor activity synthesized by a RAFT controlled/living polymerization method. This multifunctional polymer surfactant with conjugated double bond in main chain used in the interactions with cancer and normal cells. The results of these investigations indicated that PMA-RAFT polymer exhibits higher cytotoxicity, apoptotic and necrotic effects against HeLa cells while it was non-cytotoxic toward Fibroblast cells in vitro. These results allow us recommend PMA-RAFT polymer for the cancer chemotherapy applications.



\*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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