

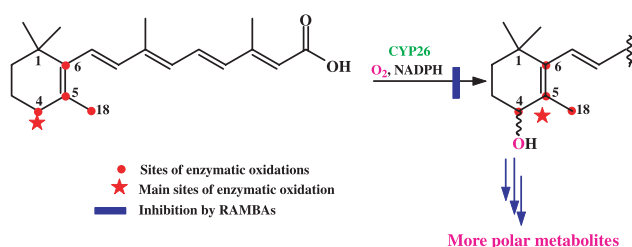
Contents

REVIEW

Retinoic acid metabolism blocking agents (RAMBAs) for treatment of cancer and dermatological diseases

pp 4323–4340

Vincent C. O. Njar,* Lalji Gediya, Puranik Purushottamachar, Pankaj Chopra, Tadas Sean Vasaitis, Aakanksha Khandelwal, Jhalak Mehta, Carlic Huynh, Aashvini Belosay and Jyoti Patel

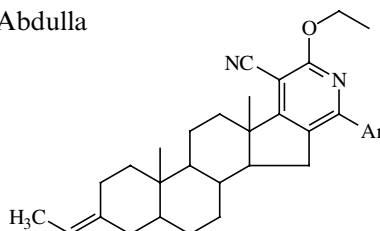


ARTICLES

Anti-inflammatory profile of some synthesized heterocyclic pyridone and pyridine derivatives fused with steroidal structure

pp 4341–4352

Abdel-Galil E. Amr* and Mohamed M. Abdulla

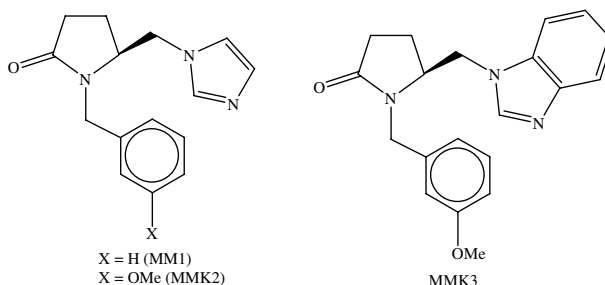


Several new heterocyclic compounds containing cyanopyridone and cyanopyridine rings fused with steroidal moiety were synthesized as anti-inflammatory agents.

Synthesis, binding studies and in vivo biological evaluation of novel non-peptide antihypertensive analogues

pp 4353–4360

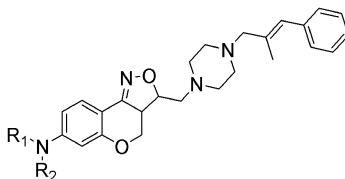
T. Mavromoustakos,* P. Moutevelis-Minakakis,* C. G. Kokotos, P. Kontogianni, A. Politi, P. Zoumpoulakis, J. Findlay, A. Cox, A. Balmforth, A. Zoga and E. Ilidromitis



**Synthesis of 7-amino-3a,4-dihydro-3H-[1]benzopyrano
[4,3-c]isoxazole derivatives displaying combined α_2 -adrenoceptor
antagonistic and 5-HT reuptake inhibiting activities**

pp 4361–4372

J. Ignacio Andrés,* Jesús Alcázar, José M. Alonso, Ana I. De Lucas, Laura Iturrino,
Ilse Biesmans and Anton A. Megens

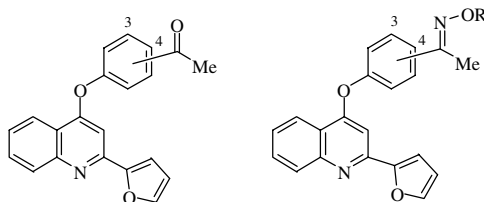


The synthesis of a series of 7-amino-3a,4-dihydro-3H-[1]benzopyranol[4,3-c]isoxazole derivatives as potential antidepressants is reported.

**Synthesis, cytotoxicity, and anti-inflammatory evaluation of 2-(furan-2-yl)-
4-(phenoxy)quinoline derivatives. Part 4**

pp 4373–4378

Yeh-Long Chen, Yue-Ling Zhao, Chih-Ming Lu,
Cherng-Chyi Tzeng* and Jih-Pyang Wang

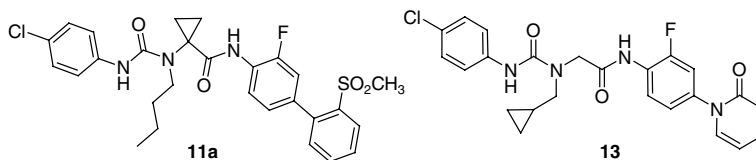


A number of 2-(furan-2-yl)-4-(phenoxy)quinoline derivatives were synthesized and evaluated for anti-inflammatory activity.

The discovery of glycine and related amino acid-based factor Xa inhibitors

pp 4379–4392

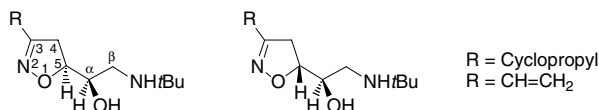
Jeffrey T. Kohrt,* Kevin J. Filipinski, Wayne L. Cody, Christopher F. Bigge,
Frances La, Kathleen Welch, Tawny Dahring, John W. Bryant, Daniele Leonard,
Gary Bolton, Lakshmi Narasimhan, Erli Zhang, J. Thomas Peterson, Staci Haarer,
Vaishali Sahasrabudhe, Nancy Janiczek, Shrilakshmi Desiraju, Mostofa Hena,
Charles Fiahpui, Neerja Saraswat, Raman Sharma, Shaoyi Sun,
Samarendra N. Maiti, Robert Leadley and Jeremy J. Edmunds



**Synthesis of enantiopure Δ^2 -isoxazoline derivatives and evaluation of their
affinity and efficacy profiles at human β -adrenergic receptor subtypes**

pp 4393–4401

Clelia Dallanocce, Giuseppe Meroni, Marco De Amici,* Carsten Hoffmann,
Karl-Norbert Klotz* and Carlo De Micheli

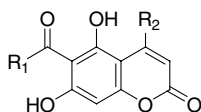


A group of enantiomerically pure 3-substituted- Δ^2 -isoxazolin-5-yl-ethanolamines was prepared and tested for their affinity and efficacy at human β_1 -, β_2 -, and β_3 -adrenergic receptor subtypes.

6-Acyl-4-aryl/alkyl-5,7-dihydroxycoumarins as anti-inflammatory agents

pp 4402–4409

Chun-Mao Lin, Sheng-Tung Huang, Fu-Wei Lee, Hsien-Saw Kuo and Mei-Hsiang Lin*

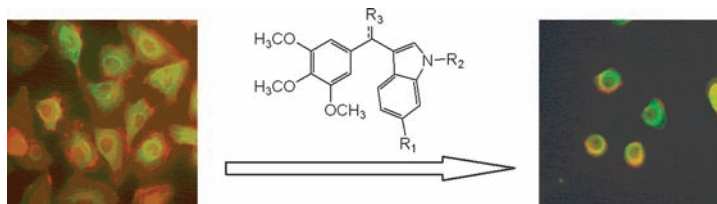
8: $R_1 = \text{CH}_2\text{C}(\text{CH}_3)_3$, $R_2 = \text{CH}_2\text{CH}_3$

A series of coumarin derivatives were synthesized and anti-inflammatory activities evaluated. Coumarin derivative **8** was the most potent derivative against NO production in LPS-induced RAW 264.7 cells with an IC_{50} value of 7.6 μM and it effectively scavenged the hydroxyl radical production by 50% at 100 μM in the electron spin resonance study.

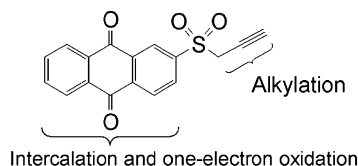
Synthesis and biological evaluation of (3,4,5-trimethoxyphenyl)indol-3-ylmethane derivatives as potential antivasular agents

pp 4410–4426

Grégory Dupeyre, Guy G. Chabot, Sylviane Thoret, Xavier Cachet, Johanne Seguin, Daniel Guénard, François Tillequin, Daniel Scherman, Michel Koch and Sylvie Michel*

**Effects of structural modification on the DNA binding properties and photo-induced cleavage reactivity of propargylic sulfones conjugated with an anthraquinone structure**

pp 4427–4432

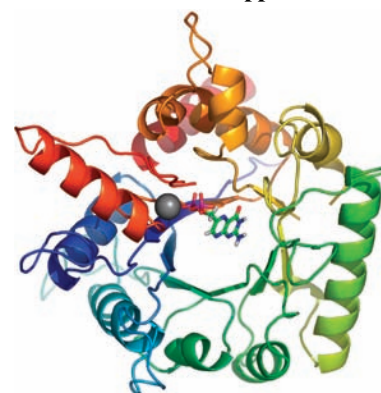
Ken-ichi Haruna, Hiroshi Kanezaki, Kazuhito Tanabe,*
Wei-Min Dai and Sei-ichi Nishimoto*

A novel propargylic sulfone derivative conjugated with an anthraquinone structure was designed and synthesized as a potent DNA cleaving agent.

**Elucidation of sulfadoxine resistance with structural models of the bifunctional *Plasmodium falciparum* dihydropterin pyrophosphokinase–dihydropteroate synthase**

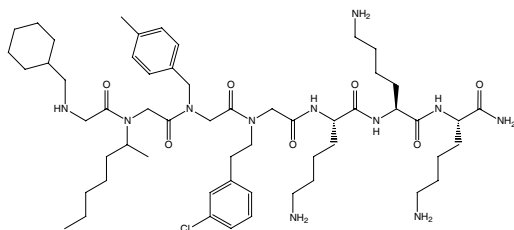
pp 4433–4443

Tjaart A. P. de Beer, Abraham I. Louw* and Fourie Joubert



Potent antibacterial lysine–peptoid hybrids identified from a positional scanning combinatorial library pp 4444–4451

Trine S. Ryge and Paul R. Hansen*

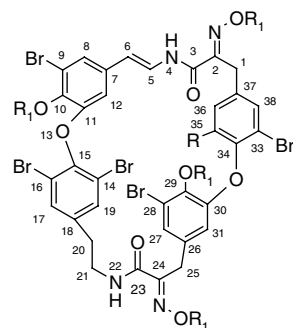


We describe the synthesis and screening of a positional scanning library made up of *N*-alkylglycines and lysines. Compounds with potent antibacterial activity and low hemolytic activity were identified including [N-(cyclohexylmethyl)glycyl]-[N-(1-methylhexyl)glycyl]-[N-(4-methylbenzyl)glycyl]-[N-(2-(3-chlorophenyl)ethyl)glycyl]-lysyl-lysyl-lysine amide.

New anticancer bastadin alkaloids from the sponge *Dendrilla cactos*

pp 4452–4457

A. Vijender Reddy, K. Ravinder, M. Narasimhulu, A. Sridevi, N. Satyanarayana, Anand K. Kondapi and Y. Venkateswarlu*



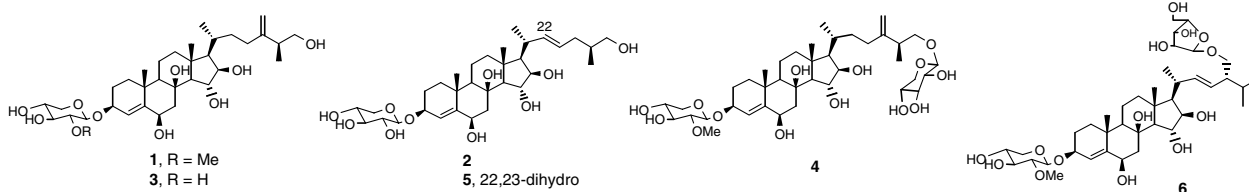
(1) R = Br, R₁ = H

(2) R = H

Structure–activity relationships of novel neuritogenic steroid glycosides from the Okinawan starfish *Linckia laevigata*

pp 4458–4465

Chunguang Han, Jianhua Qi and Makoto Ojika*

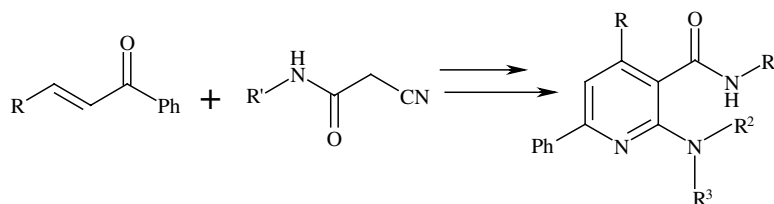


Six new steroid glycosides 1–6 were isolated from the Okinawan blue starfish *Linckia laevigata*. Their structures and neuritogenic activity were investigated.

Novel synthesis of nicotinamide derivatives of cytotoxic properties

pp 4466–4476

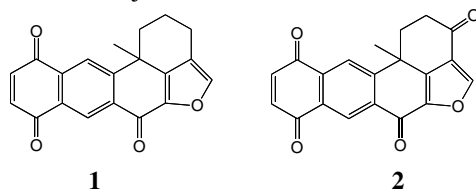
Adel S. Girgis,* Hanaa M. Hosni and Flora F. Barsoum



Antimalarial potential of xestoquinone, a protein kinase inhibitor isolated from a Vanuatu marine sponge *Xestospongia* sp.

pp 4477–4482

Dominique Laurent,* Valérie Jullian, Arnaud Parenty, Martine Knibiehler, Dominique Dorin, Sophie Schmitt, Olivier Lozach, Nicolas Lebouvier, Maryvonne Frostin, Frédéric Alby, Séverine Maurel, Christian Doerig, Laurent Meijer and Michel Sauvain

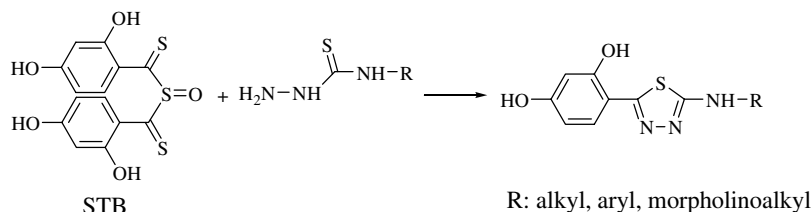


Xestoquinone **1** and halenaquinone **2** were isolated from a Vanuatu marine sponge *Xestospongia* sp. and tested for their *Plasmodium falciparum* protein kinase inhibitory activity (Pfnek-1). The antimalarial activity of xestoquinone was assessed in vitro and in vivo.

Synthesis and antiproliferative activity of N-substituted 2-amino-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazoles

pp 4483–4489

Joanna Matysiak* and Adam Opolski

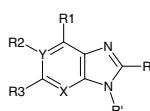


2-Amino-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole derivatives have been synthesized and evaluated for their antiproliferative activity against human cancer cell lines.

Synthesis and biological evaluation of benzimidazole derivatives as potent AMP-activated protein kinase activators

pp 4490–4518

Julie Charton,* Sophie Girault-Mizzi, Marie-Ange Debreu-Fontaine, Fabienne Foufelle, Isabelle Hainault, Jean-Guy Bizot-Espiard, Daniel-Henri Caignard and Christian Sergheraert

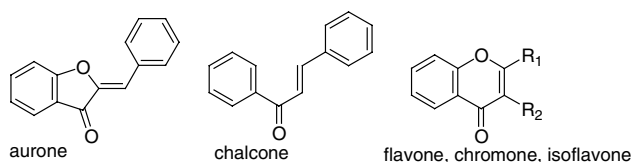


Design, synthesis and structure–activity relationships of benzimidazole derivatives as activators of the AMP-activated protein kinase are presented in this paper.

Modulation of paclitaxel transport by flavonoid derivatives in human breast cancer cells. Is there a correlation between binding affinity to NBD of P-gp and modulation of transport?

pp 4519–4525

Radka Václavíková,* Ahcene Boumendjel, Marie Ehrlichová, Jan Kovář and Ivan Gut

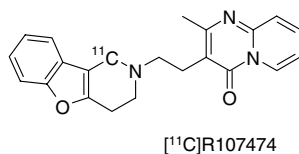


We investigated the effect of 13 flavonoid derivatives on [¹⁴C]paclitaxel transport through P-glycoprotein inhibition. A correlation between their binding affinity to NBD2 of P-gp and paclitaxel transport was performed.

Synthesis and biodistribution of [¹¹C]R107474, a new radiolabeled α_2 -adrenoceptor antagonist

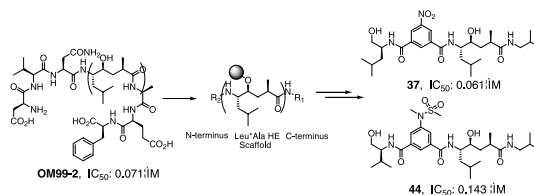
pp 4526–4534

M. Van der Mey,* A. D. Windhorst, R. P. Klok, J. D. M. Herscheid, L. E. Kennis,
F. Bischoff, M. Bakker, X. Langlois, L. Heylen, M. Jurzak and J. E. Leysen

**Design, synthesis, and evaluation of Leu*Ala hydroxyethylene-based non-peptide β -secretase (BACE) inhibitors**

pp 4535–4551

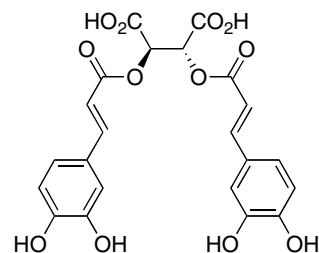
Kun Xiao, Xin Li, Jingya Li, Lanping Ma, Bin Hu, Haiping Yu, Yan Fu, Rui Wang,* Zeqiang Ma,
Beiyang Qiu, Jia Li,* Dingyu Hu, Xin Wang and Jingkang Shen*

**Design, synthesis, and biological evaluation of chicoric acid analogs as inhibitors of HIV-1 integrase**

pp 4552–4567

Trevor T. Charvat, Deborah J. Lee, W. Edward Robinson and A. Richard Chamberlin*

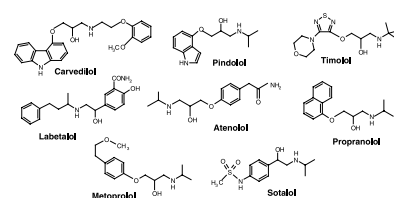
A series of analogs of the potent HIV-1 integrase (HIV IN) inhibitor chicoric acid (CA) was designed with the intention of ameliorating some of the parent natural product's undesirable properties, in particular its toxicity, instability, and poor membrane permeability. More than 70 analogs were synthesized and assayed for three types of activity: (1) inhibition of 3'-end processing and strand transfer reactions in vitro, (2) toxicity against a CD4⁺ lymphoblastoid cell line, and (3) anti-HIV activity against HIV_{LAI}.

**Antioxidant activity of β -blockers: An effect mediated by scavenging reactive oxygen and nitrogen species?**

pp 4568–4577

Ana Gomes, David Costa, José L. F. C. Lima and Eduarda Fernandes*

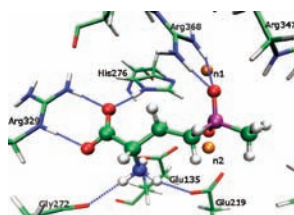
The β -blockers atenolol, labetalol, metoprolol, pindolol, propranolol, sotalol, timolol, and carvedilol were tested for their putative scavenging activity for ROS ($O_2^{\cdot-}$, H_2O_2 , HO^{\cdot} , $HOCl$, and ROO^{\cdot}) and RNS ($\cdot NO$ and $ONOO^-$). Some of the studied compounds are effective ROS and/or RNS scavengers, these effects being possibly useful in preventing oxidative damage verified in hypertension as well as in other cardiovascular diseases that frequently emerge in association with oxidative stress.



Computer-aided analysis of the interactions of glutamine synthetase with its inhibitors

pp 4578–4585

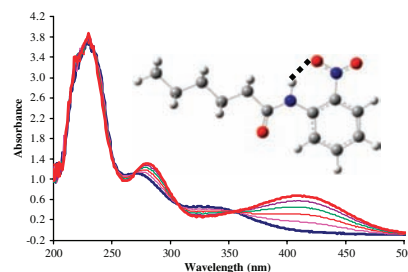
Łukasz Berlicki* and Paweł Kafarski

**On the active site for hydrolysis of aryl amides and choline esters by human cholinesterases**

pp 4586–4599

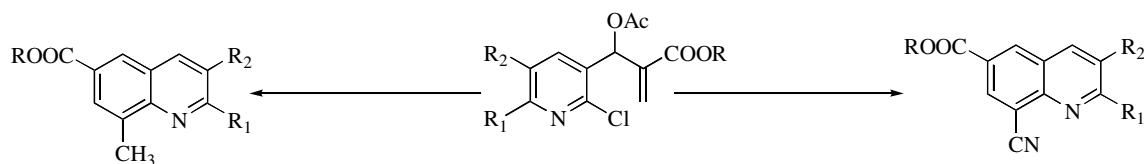
Sultan Darvesh,* Robert S. McDonald, Katherine V. Darvesh, Diane Mataija, Sam Mothana, Holly Cook, Karina M. Carneiro, Nicole Richard, Ryan Walsh and Earl Martin

A series of substituted anilides were examined as substrates for aryl acylamidase activity. The cholinesterase-catalyzed hydrolysis of anilides generally required the presence of a hydrogen-bonding moiety, such as a nitro group, in the 2-position of the aniline ring and the specificity and efficiency of hydrolysis was strongly influenced by the size of the acyl group. Larger straight chain alkyl acyl derivatives represent highly specific substrates that are efficiently hydrolyzed by the aryl acylamidase activity of butyrylcholinesterase.

**Synthesis of multisubstituted quinolines from Baylis–Hillman adducts obtained from substituted 2-chloronicotinaldehydes and their antimicrobial activity**

pp 4600–4609

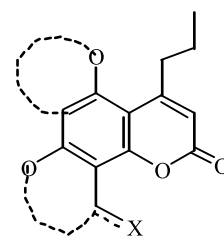
P. Narender, U. Srinivas, M. Ravinder, B. Ananda Rao, Ch. Ramesh, K. Harakishore, B. Gangadasu, U. S. N. Murthy* and V. Jayathirtha Rao*

**Pyranocoumarin, a novel anti-TB pharmacophore: Synthesis and biological evaluation against *Mycobacterium tuberculosis***

pp 4610–4626

Ze-Qi Xu,* Krzysztof Pupek, William J. Suling, Livia Enache and Michael T. Flavin

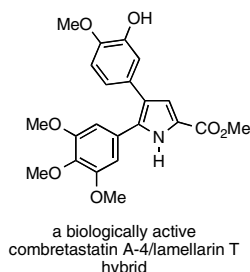
Pyranocoumarin compounds were identified to embody a novel and unique pharmacophore for anti-TB activity.

X = O, OH, NH₂

4,5-Diaryl-1*H*-pyrrole-2-carboxylates as combretastatin A-4/lamellarin T hybrids: Synthesis and evaluation as anti-mitotic and cytotoxic agents

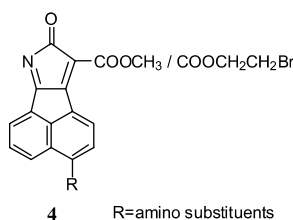
pp 4627–4638

Martin G. Banwell,* Ernest Hamel, David C. R. Hockless, Pascal Verdier-Pinard, Anthony C. Willis and David J. Wong


Design, synthesis, and antitumor evaluation of novel acenaphtho[1,2-*b*]pyrrole-carboxylic acid esters with amino chain substitution

pp 4639–4644

Fengyu Liu, Xuhong Qian,* Jingnan Cui, Yi Xiao, Rong Zhang and Gangyue Li

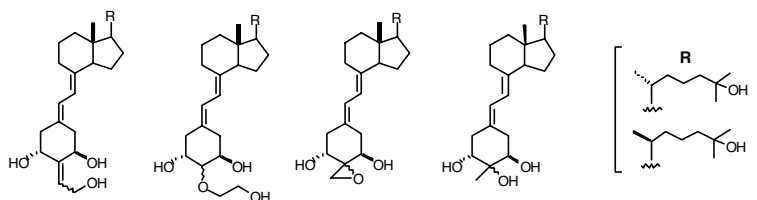


Novel acenaphtho-heterocycle 8-oxo-8*H*-acenaphtho[1,2-*b*]pyrrole-9-carboxylic acid esters and their amino derivatives were synthesized and evaluated for their antitumor activities against cell lines of A549 and P388.

Analogues of 1 α ,25-dihydroxyvitamin D₃ with high potency in induction of osteoclastogenesis and prevention of dendritic cell differentiation: Synthesis and biological evaluation of 2-substituted 19-norvitamin D analogues

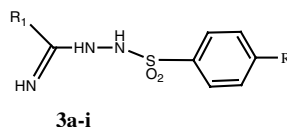
pp 4645–4656

Mika Shimazaki,* Yukiko Miyamoto, Keiko Yamamoto, Sachiko Yamada, Masamichi Takami, Toshimasa Shinki, Nobuyuki Udagawa and Masato Shimizu*

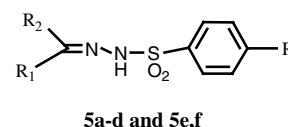

Synthesis, anti-inflammatory and analgesic activity evaluation of some amidine and hydrazone derivatives

pp 4657–4663

Sham M. Sondhi,* Monica Dinodia and Ashok Kumar



Where R₁, R are various substituents



Where R₁, R₂ and R are various substituents

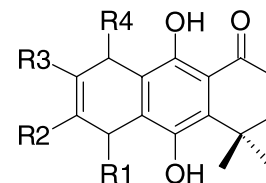
A number of amidine derivatives (3a–i) were synthesized by condensation of cyanopyridine and cyanopyrazine with sulfonylhydrazides in the presence of sodium methoxide. 2-Acetylpyridine and 4-acetylpyridine were condensed with sulfonylhydrazides by microwave irradiation in solid phase to give corresponding hydrazones (5a–d). Indole-3-carboxaldehyde was condensed with sulfonylhydrazides by refluxing in acetic acid to give corresponding condensation products (5e and f). Anti-inflammatory activity evaluation was carried out using carrageenin-induced paw oedema assay and compounds 3e,f and 5e exhibited good anti-inflammatory activity. Analgesic activity evaluation was carried out using acetic acid writhing assay and compounds 3a,c,e and 5f showed good analgesic activity.

Effects of 9,10-dihydroxy-4,4-dimethyl-5,8-dihydro-1(4H)-anthracenone derivatives on tumor cell respiration

pp 4664–4669

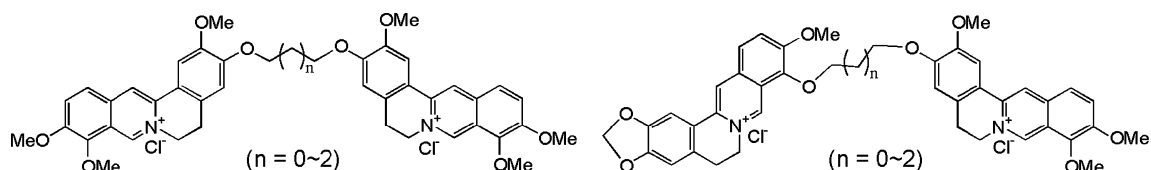
Ramiro Araya-Maturana,* Wilson Cardona, Bruce K. Cassels, Tomás Delgado-Castro, Jorge Ferreira, Dante Miranda, Mario Pavani, Hernán Pessoa-Mahana, Jorge Soto-Delgado and Boris Weiss-López

A series of tricyclic hydroquinones incorporating a carbonyl group in the *ortho* position with regard to the phenol function were tested as inhibitors of oxygen uptake against the TA3 mouse carcinoma cell line and its multidrug-resistant variant TA3-MTX-R, the title compound being the most active. This compound also exhibits low micromolar dose-dependent growth inhibition of the human tumor U937 (human monocytic leukemia) cell line.

**Spacer length and attaching position-dependent binding of synthesized protoberberine dimers to double-stranded DNA**

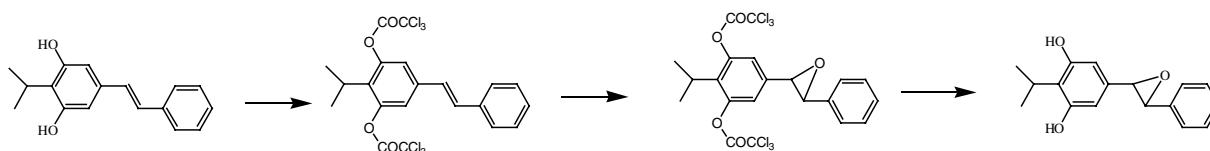
pp 4670–4676

Yu-Hua Long, Li-Ping Bai, Yong Qin, Ji-Yan Pang, Wen-Hua Chen,* Zongwei Cai, Zun-Le Xu and Zhi-Hong Jiang*

**A novel antimicrobial epoxide isolated from larval *Galleria mellonella* infected by the nematode symbiont, *Photorhabdus luminescens* (Enterobacteriaceae)**

pp 4677–4681

Kaiji Hu,* Jianxiong Li, Bin Li, John M. Webster and Genhui Chen



A novel, naturally occurring antimicrobial epoxide, 2-isopropyl-5-(3-phenyl-oxiranyl)-benzene-1,3-diol, was isolated and its structure was determined with spectroscopic analysis and confirmed by chemical synthesis.

OTHER CONTENTS**Bioorganic & Medicinal Chemistry Reviews and Perspectives**

pp 4682–4684

Summary of instructions to authors

p I

*Corresponding author

Supplementary data available via ScienceDirect

COVER

2006: The cover figure shows a synthetic multifunctional pore that is composed of rigid-rod staves (para-octiphenyls, tan) and beta-sheet hoops (arrows) and can be activated with external ligands (fullerenes, golden spheres) and closed with internal blockers (alpha-helix, red ribbon) [Gorteau, V.; Bollot, G.; Mareda, J.; Pasini, D.; Tran, D.-H.; Lazar, A. N.; Coleman, A. W.; Sakai, N.; Matile, S. *Bioorg. Med. Chem.* **2005**, *13*, 5171–5180].



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