

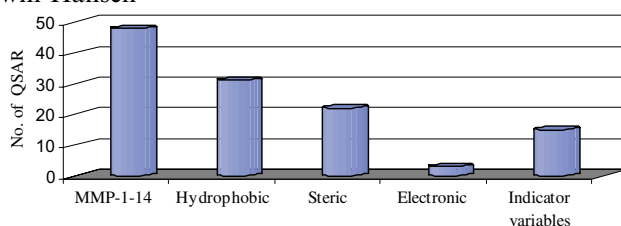
Contents

REVIEW

Matrix metalloproteinases (MMPs): Chemical–biological functions and (Q)SARs

pp 2223–2268

Rajeshwar P. Verma* and Corwin Hansch



The review highlights from the classification of this enzyme to the clinical trials of their inhibitors. A total number of 92 QSAR models (44 published and 48 new QSAR models) have also been presented. Contributions of different descriptors in the derivation of 48 new QSAR models for MMP-1–14 are shown in the figure.

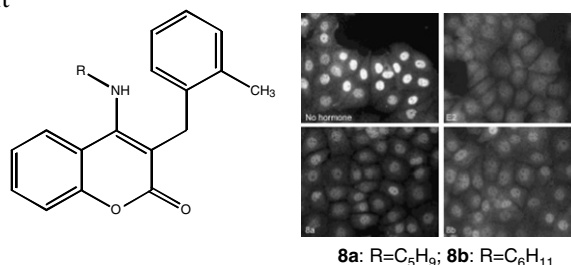
ARTICLES

Synthesis, structure, and estrogenic activity of 4-amino-3-(2-methylbenzyl)coumarins on human breast carcinoma cells

pp 2269–2282

Yves Jacquot,* Ioanna Laïos, Anny Cleeren, Denis Nonclercq, Laurent Bermont, Bernard Refouvelet, Kamal Boubekeur, Alain Xicluna, Guy Leclercq and Guy Laurent

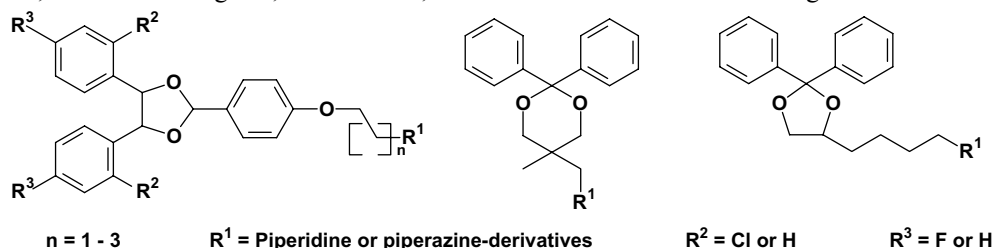
We describe the synthesis of substituted 4-amino-3-(2-methylbenzyl)coumarins tested toward estrogenic pathways in breast cancer cells. The nature of the N-substituents allows one to distinguish subtly transcriptional activity from down-regulation and cell proliferation.



New 1,3-dioxolane and 1,3-dioxane derivatives as effective modulators to overcome multidrug resistance

pp 2283–2297

Matthias Schmidt,* Johannes Ungvári, Julia Glöde, Bodo Dobner and Andreas Langner



Novel 2,2-diphenyl-1,3-dioxolane, 2,2-diphenyl-1,3-dioxane, and 4,5-diphenyl-1,3-dioxolane derivatives with variable linker and basic moiety show a high activity to reverse MDR in human Caco-2 cells.

Carbonic anhydrase and matrix metalloproteinase inhibitors.

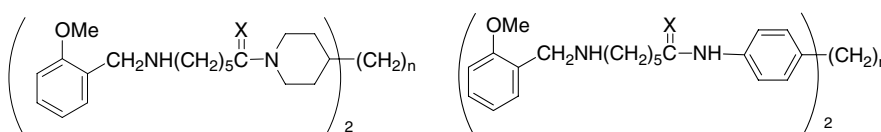
pp 2298–2311

Inhibition of human tumor-associated isozymes IX and cytosolic isozyme I and II with sulfonylated hydroxamatesElisa Nuti, Elisabetta Orlandini, Susanna Nencetti, Armando Rossello,*
Alessio Innocenti, Andrea Scozzafava and Claudiu T. Supuran*

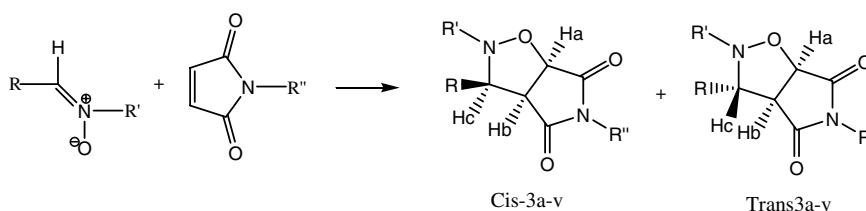
The synthesis and biological evaluation of two series of hydroxamates are reported. Some of them proved to be potent and selective inhibitors of hCA II, also active on gelatinases in the micromolar range.

Structure–activity relationships of methoctramine-related polyamines as muscarinic antagonist:

pp 2312–2321

Effect of replacing the inner polymethylene chain with cyclic moietiesVincenzo Tumiatti,* Anna Minarini, Andrea Milelli, Michela Rosini, Michela Buccioni, Gabriella Marucci,
Carla Ghelardini, Cristina Bellucci and Carlo Melchiorre**Synthesis and structure–antibacterial activity relationship investigation of isomeric 2,3,5-substituted perhydropyrrolo[3,4-*d*]isoxazole-4,6-diones**

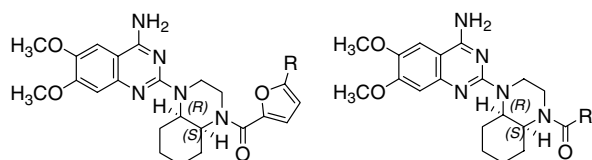
pp 2322–2333

Hikmet Agirbas,* Selahaddin Guner, Fatma Budak, Sema Keceli, Fatma Kandemirli, Nathaly Shvets,
Vasyl Kovalishyn and Anatholy Dimoglo*

A series of isomeric 2,3,5-substituted perhydropyrrolo[3,4-*d*]isoxazole-4,6-diones (*cis*-**3a-v** and *trans*-**3a-v**) were prepared in order to investigate their antibacterial activities. Some of them showed promising activity.

Synthesis and α_1 -adrenoceptor antagonist activity of derivatives and isosters of the furan portion of (+)-cyclazosin

pp 2334–2345

Gianni Sagratini, Piero Angeli, Michela Buccioni, Ugo Gulini, Gabriella Marucci,
Carlo Melchiorre, Amedeo Leonardi, Elena Poggesi and Dario Giardinà*

Compound (+)-**3**, R = CH₃, improved the functional α_{1B} -adrenoceptor selectivity of (+)-cyclazosin.

The effect of 5-substitution in the pyrimidine ring of dUMP on the interaction with thymidylate synthase: Molecular modeling and QSAR

pp 2346–2358

Adam Jarmuła,* Piotr Cieplak, Tadeusz M. Krygowski and Wojciech Rode

Molecular modeling and QSAR studies of the effect of 5-substitution in the pyrimidine ring of dUMP on binding characteristics and affinity for thymidylate synthase are reported.

Novel cationic and neutral glycocholic acid and polyamine conjugates able to inhibit transporters involved in hepatic and intestinal bile acid uptake

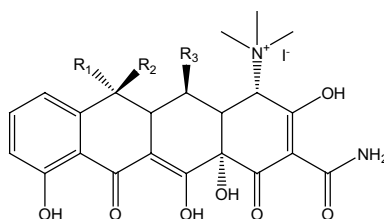
pp 2359–2367

Marta Vicens, Manuel Medarde, Rocio I. R. Macias,
Monica G. Larena, Antonio Villafaina,
Maria A. Serrano and Jose J. G. Marin*

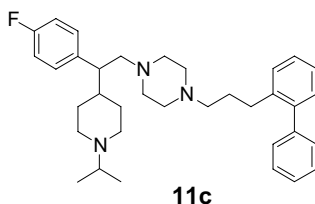
Glycocholic acid and polyamine conjugates able to inhibit bile acid transporters. Potential usefulness to protect hepatocytes against toxins taken up through these transporters or to inhibit intestinal bile acid absorption.

Synthesis and in vitro evaluation of targeted tetracycline derivatives: Effects on inhibition of matrix metalloproteinases

pp 2368–2374

Aurélien Vidal,* Massimo Sabatini, Gaëlle Rolland-Valognes, Pierre Renard,
Jean-Claude Madelmont and Emmanuelle Mounetou**Novel piperazines: Potent melanocortin-4 receptor antagonists with anxiolytic-like activity**

pp 2375–2385

Dai Nozawa,* Taketoshi Okubo, Takaaki Ishii, Kazuaki Takamori, Shigeyuki Chaki,
Shigeru Okuyama and Atsuro Nakazato

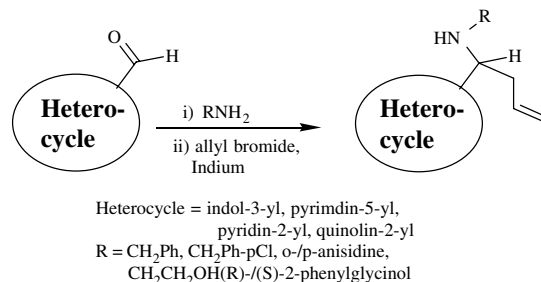
11c

Syntheses and anti-cancer activities of 2-[1-(indol-3-yl-/pyrimidin-5-yl-/pyridine-2-yl-/quinolin-2-yl)-but-3-enylamino]-2-phenyl-ethanols

pp 2386–2395

Palwinder Singh,* Pervinder Kaur, Vijay Luxami, Satwinderjit Kaur and Subodh Kumar*

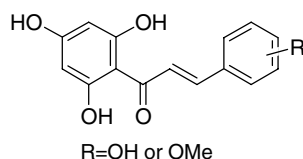
Indium mediated allylation of Schiff bases provides a convenient route to the target molecules. Investigations of anti-cancer activities on these compounds identify two potent anti-cancer agents.



Synthesis and evaluation of 2',4',6'-trihydroxychalcones as a new class of tyrosinase inhibitors

pp 2396–2402

Nishida Jun, Gao Hong and Kawabata Jun*

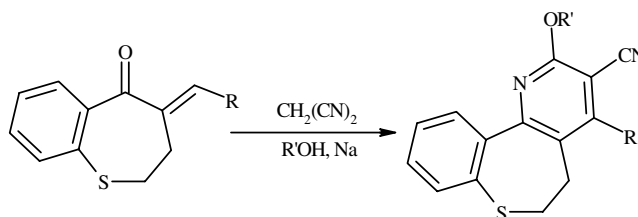


A series of 2',4',6'-trihydroxychalcones were synthesized and their tyrosinase. Inhibitory effects were examined.

Novel synthesis of [1]-benzothiepine[5,4-b]pyridine-3-carbonitriles and their anti-inflammatory properties

pp 2403–2413

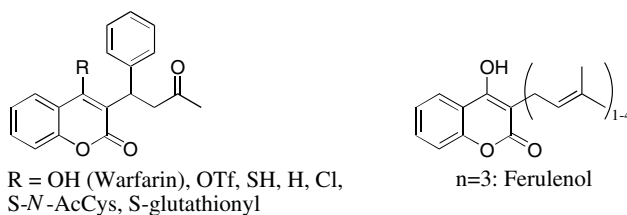
Adel S. Girgis,* Nawal Mishriky, Mohey Ellithey, Hanaa M. Hosni and Hanaa Farag



Synthesis and structure–activity relationships of novel warfarin derivatives

pp 2414–2420

Markus Gebauer*



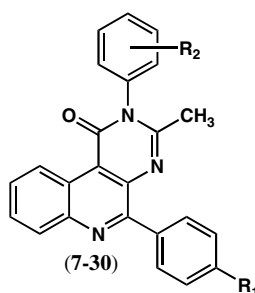
Synthesis, pharmacological evaluation and electrochemical studies of novel 6-nitro-3,4-methylenedioxyphenyl-*N*-acylhydrazone derivatives: Discovery of LASSBio-881, a new ligand of cannabinoid receptors pp 2421–2433

Carolina D. Duarte, Jorge L. M. Tributino, Daniel I. Lacerda, Marina V. Martins, Magna S. Alexandre-Moreira, Fernando Dutra, Etelvino J. H. Bechara, Francine S. De-Paula, Marilia O. F. Goulart, Juliano Ferreira, João B. Calixto, Marise P. Nunes, Alvaro L. Bertho, Ana Luisa P. Miranda, Eliezer J. Barreiro and Carlos A. M. Fraga*

We describe herein the discovery of LASSBio-881 (**3c**) as a novel in vivo antinociceptive, anti-inflammatory, and in vitro antiproliferative and antioxidant compound, with a cannabinoid ligand profile.

Synthesis and biological activity of 2,5-diaryl-3-methylpyrimido[4,5-*c*]quinolin-1(2*H*)-one derivatives pp 2434–2440

Kamel Metwally,* Omar Aly, Enayat Aly, Abhijit Banerjee, Rudravajhala Ravindra and Susan Bane

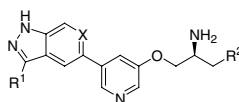


R1 = Cl, Br.

R2 = H, 4-F, 2-Cl, 3-Cl, 4-Cl, 2-Br, 3-Br, 4-Br, 2-CH3, 4-CH3, 2-OCH3, 4-OCH3.

Design and synthesis of pyridine–pyrazolopyridine-based inhibitors of protein kinase B/Akt pp 2441–2452

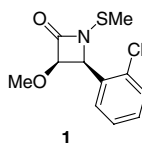
Gui-Dong Zhu,* Jianchun Gong, Viraj B. Gandhi, Keith Woods, Yan Luo, Xuesong Liu, Ran Guan, Vered Klinghofer, Eric F. Johnson, Vincent S. Stoll, Mulugeta Mamo, Qun Li, Saul H. Rosenberg and Vincent L. Giranda



We have designed and synthesized a series of potent pyridine–pyrazolopyridine-based inhibitors of protein kinase B/Akt. The best compound in this series showed 0.6 nM IC₅₀ against Akt and 180-fold selectivity over protein kinase A (PKA). The structure–activity relationships of these compounds and their structural features when bound to PKA are also discussed.

N-thiolated β-lactams: Studies on the mode of action and identification of a primary cellular target in *Staphylococcus aureus* pp 2453–2467

Kevin D. Revell, Bart Heldreth, Timothy E. Long, Seyoung Jang and Edward Turos*




Results are presented from studies on the mechanism of action and the elucidation of a cellular target of *N*-methylthio β-lactam antibiotic **1** in *Staphylococcus aureus*.

OTHER CONTENTS

Bioorganic & Medicinal Chemistry Reviews and Perspectives
Summary of instructions to authors

pp 2468–2470
p I

*Corresponding author

+ Supplementary data available via ScienceDirect

COVER

Blockage of fatty acid synthesis in *S. aureus* by N-thiolated β -lactam antibiotics [Revell, K. D.; Heldreth, B.; Long, T. E.; Jang, S.; Turos, E. *Bioorg. Med. Chem.* **2007**, *15*, 2453–2467].

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