

Contents

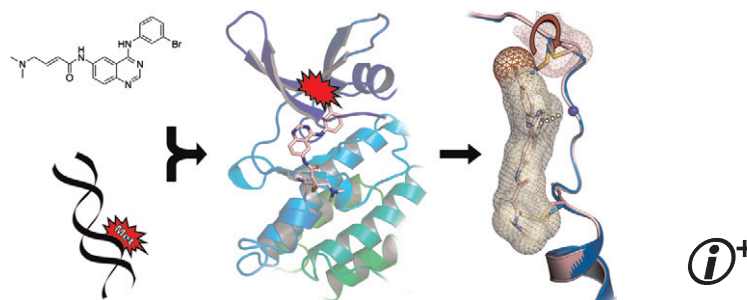
ARTICLES

Structural insights into how irreversible inhibitors can overcome drug resistance in EGFR

pp 3482–3488

Anja Michalczyk, Sabine Klüter, Haridas B. Rode, Jeffrey R. Simard, Christian Grütter, Matthias Rabiller and Daniel Rauh*

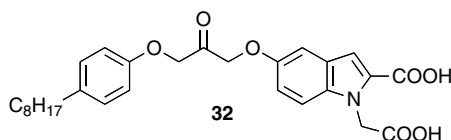
Defeating drug resistance in oncogenic EGFR by irreversible inhibitors.



1-(2-Carboxyindol-5-yloxy)propan-2-ones as inhibitors of human cytosolic phospholipase A₂α: Synthesis, biological activity, metabolic stability, and solubility

pp 3489–3500

Alexandra Fritsche, Alwine Schulze Elfringhoff, Jörg Fabian and Matthias Lehr*

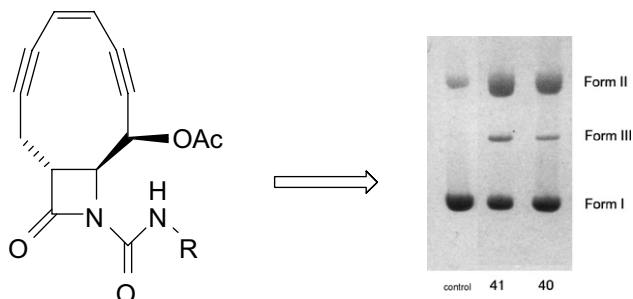


Synthesis and DNA-cleaving activity of lactenediynes conjugated with DNA-complexing moieties

pp 3501–3518

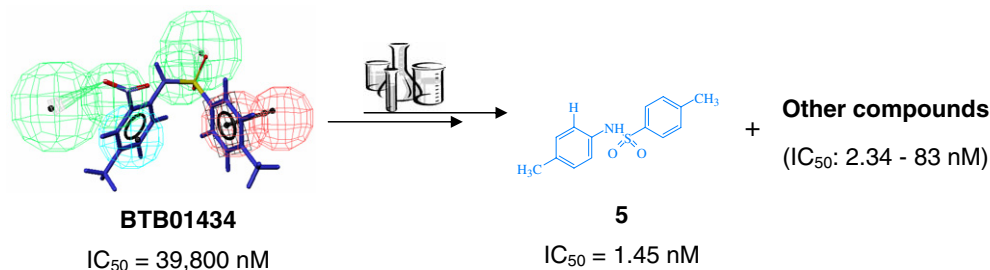
Luca Banfi,* Andrea Basso, Elisabetta Bevilacqua, Valentina Gandolfo, Giuseppe Giannini, Giuseppe Guanti,* Loana Musso, Monica Paravidino and Renata Riva

Lactenediynes activated as azetidiny ureas and bearing DNA-complexing substructures R are able to afford single and double strand cleavage of plasmid DNA at sub-micromolar concentrations.

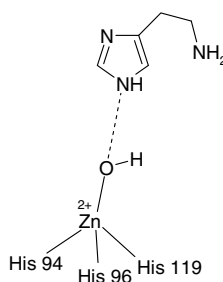


Potent anti-prostate cancer agents derived from a novel androgen receptor down-regulating agent

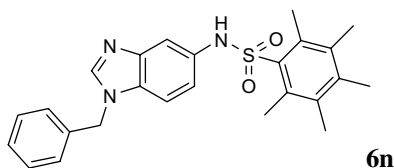
pp 3519–3529

Puranik Purushottamachar, Aakanksha Khandelwal, Tadas S. Vasaitis,
Robert D. Bruno, Lalji K. Gediya and Vincent C. O. Njar***Carbonic anhydrase activators: Activation of the human tumor-associated isozymes IX and XII with amino acids and amines**

pp 3530–3536

Silvia Pastorekova, Daniela Vullo, Isao Nishimori, Andrea Scozzafava,
Jaromir Pastorek and Claudiu T. Supuran***N-1H-Benzimidazol-5-ylbenzenesulfonamide derivatives as potent hPXR agonists**

pp 3537–3549

Cindy Benod, Guy Subra, Virginie Nahoum, Aude Mallavialle,
Jean-François Guichou, Julien Milhau, Samuel Roblés, William Bourguet,
Jean-Marc Pascussi, Patrick Balaguer and Alain Chavanieu*

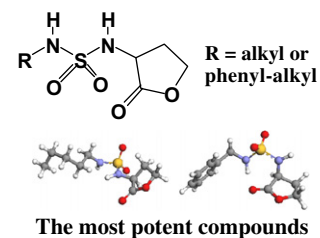
In this study, we identified compound **6n** as a potent agonist of hPXR with active concentration in the subnanomolar range.

**Synthetic homoserine lactone-derived sulfonylureas as inhibitors of *Vibrio fischeri* quorum sensing regulator**

pp 3550–3556

Marine Frezza, Laurent Soulère, Sylvie Reverchon, Nicolas Guiliani,
Carlos Jerez, Yves Queneau and Alain Doutheau*

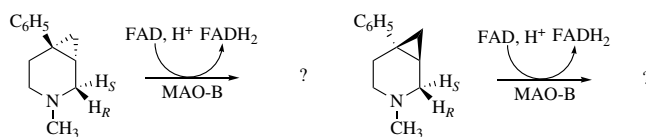
A series of 9 homoserine lactone-derived sulfonylureas, were prepared and found to inhibit the acyl-homoserine lactones-dependent *Vibrio fischeri* quorum sensing regulator. Molecular modelling suggested that the inhibitory activity could be related to the perturbation of the hydrogen-bond network in the ligand–protein complexes.



Stereochemical studies on the novel monoamine oxidase B substrates (1*R*,6*S*)- and (1*S*,6*R*)-3-methyl-6-phenyl-3-aza-bicyclo[4.1.0]heptane

pp 3557–3564

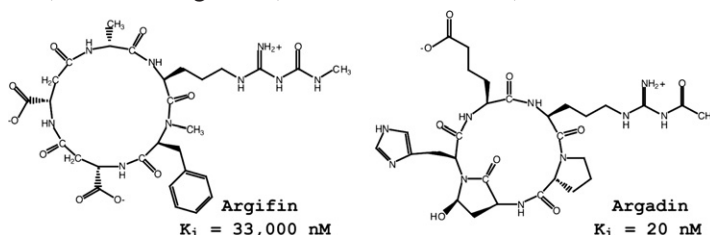
Philippe Bissel,* Ashraf Khalil, John M. Rimoldi, Kazuo Igarashi, Dale Edmondson, Anthony Miller and Neal Castagnoli, Jr.



Computational analysis of the binding affinities of the natural-product cyclopentapeptides argifin and argadin to chitinase B from *Serratia marcescens*

pp 3565–3579

Hiroaki Gouda,* Yuichi Yanai, Akihiro Sugawara, Toshiaki Sunazuka, Satoshi Ōmura and Shuichi Hirono



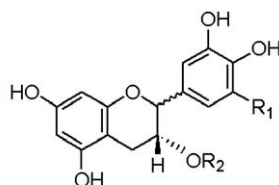
A possible cause of the different binding affinities of argifin and argadin with Chitinase B was investigated using the MM-PBSA free-energy analysis.



Catechin gallates are NADP⁺-competitive inhibitors of glucose-6-phosphate dehydrogenase and other enzymes that employ NADP⁺ as a coenzyme

pp 3580–3586

Eui Seok Shin, Jiyoung Park, Jae-Min Shin, Doocho Cho, Si Young Cho, Dong Wook Shin, Mira Ham, Jae Bum Kim and Tae Ryong Lee*



R₁ : H or OH

R₂ : H IC₅₀ >> 1000

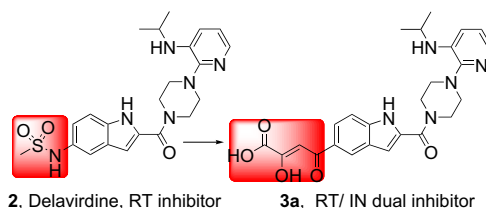
R₂ : 3,4,5-trihydroxybenzoyl IC₅₀ = 0.18 μM ~ 0.25 μM



Design and synthesis of dual inhibitors of HIV reverse transcriptase and integrase: Introducing a diketoacid functionality into delavirdine

pp 3587–3595

Zhengqiang Wang* and Robert Vince*



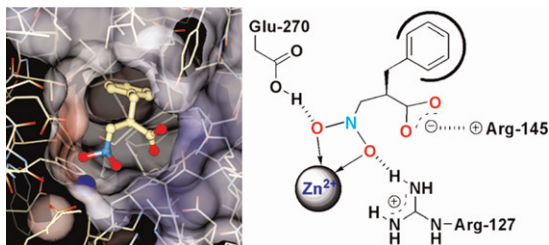
2, Delavirdine, RT inhibitor

3a, RT/ IN dual inhibitor

Nitro as a novel zinc-binding group in the inhibition of carboxypeptidase A

pp 3596–3601

Si-Hong Wang, Shou-Feng Wang, Wei Xuan, Zong-Hao Zeng, Jing-Yi Jin,* Jie Ma and Guan Rong Tian*

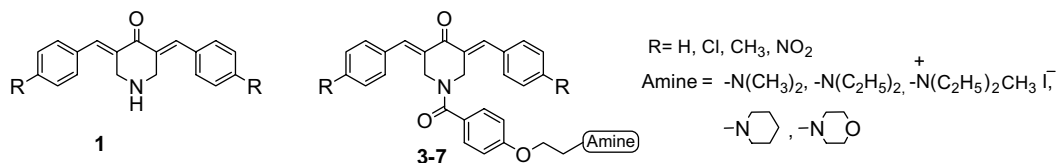


X-ray crystallography of carboxypeptidase A-(*R*)-2-benzyl-3-nitropropanoic acid complex disclosed that the nitro group chelate the zinc ion in the active site of CPA in an *O,O'*-bidentate fashion.

***N*-Aroyl-3,5-bis(benzylidene)-4-piperidones: A novel class of antimycobacterial agents**

pp 3602–3607

Umashankar Das, Swagatika Das, Brian Bandy, James P. Stables and Jonathan R. Dimmock*

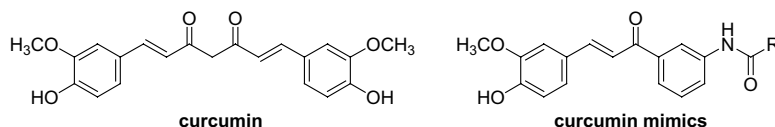


A number of 3,5-bis(benzylidene)-4-piperidones **1** and related *N*-4-(2-aminoethoxy)phenylcarbonyl analogs **3–7** were screened against *Mycobacterium tuberculosis* H₃₇Rv and for neurotoxicity in mice. A number of lead molecules were identified as potent antitubercular agents which are well tolerated in mice.

Synthesis of curcumin mimics with multidrug resistance reversal activities

pp 3608–3615

Yumi Um, Sungsik Cho, Ho Bum Woo, Yong Kee Kim, Hanna Kim, Jungyeob Ham, Su-Nam Kim, Chan Mug Ahn* and Seokjoon Lee*

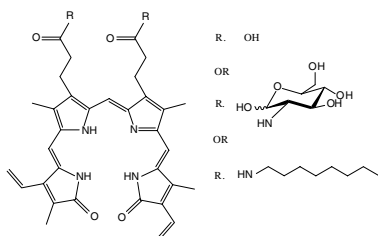


The unsymmetrical curcumin mimics with various amide moieties were synthesized and evaluated their multidrug resistance (MDR) reversal activities in MDR cell line KBV20C.

**In vitro permeability and metabolic stability of bile pigments and the effects of hydrophilic and lipophilic modification of biliverdin**

pp 3616–3625

Andrew C. Bulmer,* Joanne T. Blanchfield, Jeff. S. Coombes and Istvan Toth

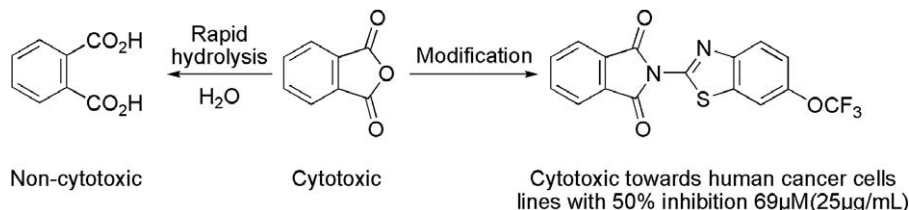


Hydrophilic and lipophilic conjugates of biliverdin were prepared. Native and conjugated bile pigments were then tested in Caco-2 cell permeability and stability assays.



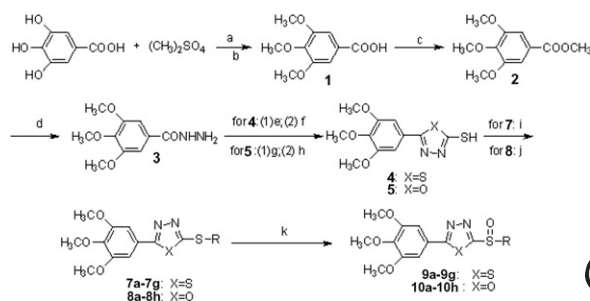
Synthesis and anti-cancer activity of benzothiazole containing phthalimide on human carcinoma cell lines pp 3626–3631

Stanton Hon Lung Kok, Roberto Gambari, Chung Hin Chui, Marcus Chun Wah Yuen, Eva Lin, Raymond Siu Ming Wong, Fung Yi Lau, Gregory Yin Ming Cheng, Wing Sze Lam, Sau Hing Chan, Kim Hung Lam, Chor Hing Cheng, Paul Bo Shan Lai, Michael Wing Yiu Yu, Filly Cheung,* Johnny Cheuk On Tang* and Albert Sun Chi Chan*

**Synthesis and antifungal activity of novel sulfoxide derivatives containing trimethoxyphenyl substituted 1,3,4-thiadiazole and 1,3,4-oxadiazole moiety** pp 3632–3640

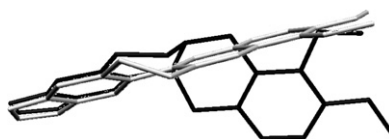
Fang Liu, Xiao-Qiong Luo, Bao-An Song,* Pinaki S. Bhadury, Song Yang, Lin-Hong Jin, Wei Xue and De-Yu Hu

Selective oxidation of sulfides **7** or **8** to sulfoxides **9** or **10** is achieved by *m*CPBA in dichloromethane. The structures of compounds **9** or **10** are confirmed by elemental analysis, IR, and ¹H NMR. The bioassay results showed that title compound **10a** possessed high antifungal activities with EC₅₀ values ranging from 19.91 to 63.97 µg/mL. The mechanism of action of **10a** against *Sclerotinia sclerotiorum* was studied.

**Antioxidant and cytotoxic activities of canadine: Biological effects and structural aspects**

pp 3641–3651

Estela R. Correché, Sebastian A. Andujar, Rita R. Kurdelas, María J. Gómez Lechón, Mónica L. Freile and Ricardo D. Enriz*

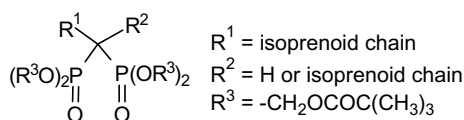


The cytotoxic effects of four alkaloids, berberine, canadine, anonaine, and antioquine were evaluated. The antioxidant activity of canadine, combined with its low-toxic effect, indicated that this alkaloid is a promising candidate for a novel antioxidant agent. The figure shows the stereoview of overlapping of berberine (light gray) and canadine (black).

Pivaloyloxymethyl-modified isoprenoid bisphosphonates display enhanced inhibition of cellular geranylgeranylation

pp 3652–3660

Andrew J. Wiemer, Jose S. Yu, Larry W. Shull, Rocky J. Barney, Brian M. Wasko, Kimberly M. Lamb, Raymond J. Hohl and David F. Wiemer*

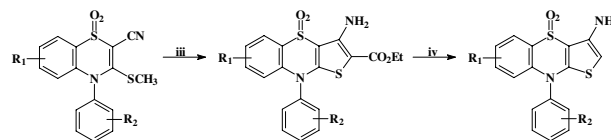


Synthesis, antimalarial activity, structure–activity relationship analysis of thieno-[3,2-*b*]benzothiazine *S,S*-dioxide analogs

pp 3661–3674

Arthur Barazarte, José Camacho, José Domínguez, Gricela Lobo, Neira Gamboa, Juan Rodrigues, Mario V. Capparelli, Ángel Álvarez-Larena, Sebastian Andujar, Daniel Enriz and Jaime Charris*

An improved procedure for the synthesis of 3-amino-9-arylsubstituted-thieno[3,2-*b*]benzothiazine *S,S*-dioxide 2-decarboxylated is reported. A conformational and electronic study on the most representative compounds of this series was carried out using ab initio calculations. A comparative study between thieno-[2,3-*b*]benzothiazine *S,S*-dioxide and thieno-[3,2-*b*]quinolones analogs could explain the different chemical behavior obtained for these compounds. Thieno-[3,2-*b*]benzothiazine *S,S*-dioxide derivatives were investigated for their abilities to inhibit β -hematin formation, hemoglobin hydrolysis and in vivo for their efficacy in rodent *Plasmodium berghei*.



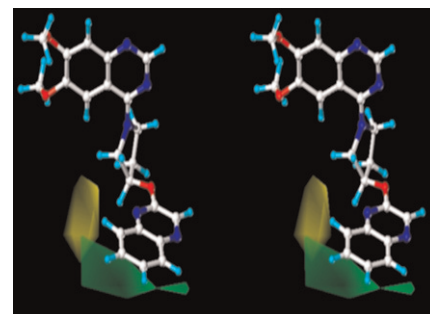
iii: $\text{HSCH}_2\text{CO}_2\text{Et}$, Et_3N , EtOH , Δ ; iv: NaOH , KOH , LiOH or HCl , Δ

CoMFA and HQSAR studies on 6,7-dimethoxy-4-pyrrolidylquinazoline derivatives as phosphodiesterase10A inhibitors

pp 3675–3686

Shridhar S. Kulkarni, Maulik R. Patel and Tanaji T. Talele*

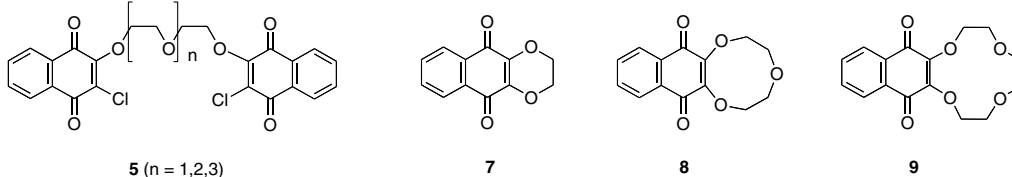
CoMFA and HQSAR study was carried out on a series of quinazoline inhibitors of phosphodiesterase10A (PDE10A). The CoMFA and HQSAR models showed excellent capabilities for the design of new PDE10A inhibitors.



Studies on quinones. Part 43: Synthesis and cytotoxic evaluation of polyoxyethylene-containing 1,4-naphthoquinones

pp 3687–3693

Jaime A. Valderrama,* Hilda Leiva, Jaime A. Rodríguez, Cristina Theoduloz and Guillermo Schmeda-Hirshmann

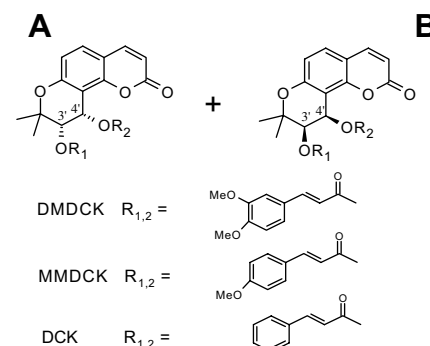


Naphthoquinones 2,3-disubstituted with chlorine and oxyethylene groups (**5**, **7–9**) were prepared from 2,3-dichloro- and 2,3-dimethoxy-1,4-naphthoquinone. These compounds were tested on normal human fibroblasts and on a panel of four human cancer cell lines. Antitumor activities, which were in the range of IC_{50} 1.3–89.5 μM , are discussed in terms of LUMO energy, lipophilicity, and size of the polyoxyethylene moiety.

Methoxylation of 3',4'-aromatic side chains improves P-glycoprotein inhibitory and multidrug resistance reversal activities of 7,8-pyrancoumarin against cancer cells

pp 3694–3703

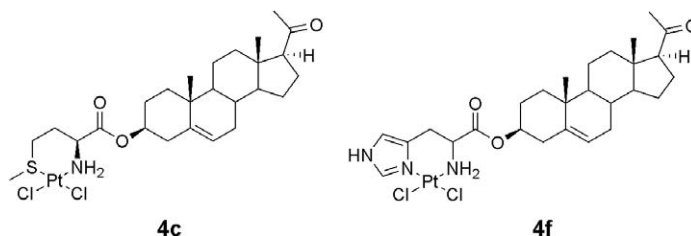
Wang-Fun Fong,* Xiao-Ling Shen, Christoph Globisch, Michael Wiese, Guang-Ying Chen, Guo-Yuan Zhu, Zhi-Ling Yu, Anfernee Kai-Wing Tse and Ying-Jie Hu



Platinum(II) complexes with steroidal esters of L-methionine and L-histidine: Synthesis, characterization and cytotoxic activity

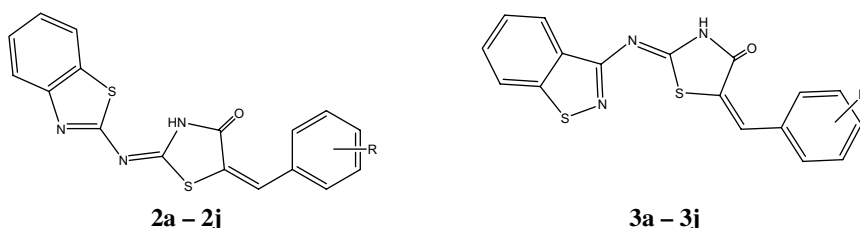
pp 3704–3713

Miroslav Kvasnica, Milos Budesinsky, Jana Swaczynova, Vladimir Pouzar and Ladislav Kohout*

**2-Heteroarylimino-5-benzylidene-4-thiazolidinones analogues of 2-thiazolylimino-5-benzylidene-4-thiazolidinones with antimicrobial activity: Synthesis and structure–activity relationship**

pp 3714–3724

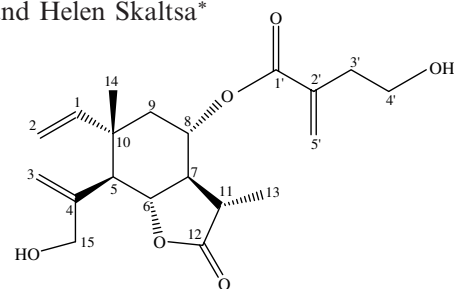
Paola Vicini,* Athina Geronikaki, Matteo Incerti, Franca Zani, John Dearden and Mark Hewitt

**A novel sesquiterpene lactone from *Centaurea pullata*: Structure elucidation, antimicrobial activity, and prediction of pharmacokinetic properties**

pp 3725–3731

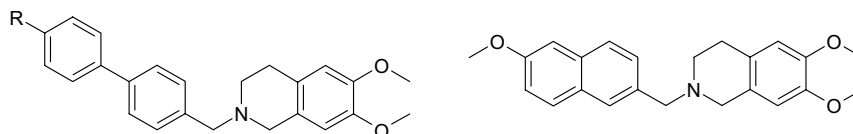
Samah Djeddi, Anastasia Karioti, Marina Sokovic, Catherine Koukoulitsa and Helen Skaltsa*

8 α -O-(4-Hydroxy-2-methylenebutanoyloxy)melitensine. A novel elemanolide with an α -methyl- γ -lactone moiety isolated from *Centaurea pullata*.

8 α -O-(4-hydroxy-2-methylenebutanoyloxy) melitensine.**4-Biphenyl and 2-naphthyl substituted 6,7-dimethoxytetrahydroisoquinoline derivatives as potent P-gp modulators**

pp 3732–3743

Nicola Antonio Colabufo,* Francesco Berardi, Mariangela Cantore, Maria Grazia Perrone, Marialessandra Contino, Carmela Inglese, Mauro Niso, Roberto Perrone, Amalia Azzariti, Grazia Maria Simone and Angelo Paradiso



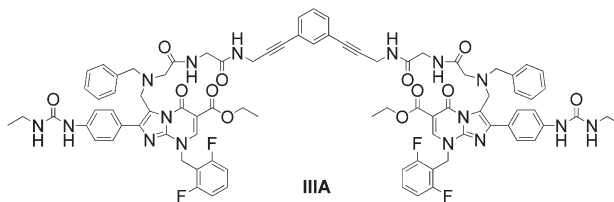
Biphenyl **4c** (R = H, EC₅₀ = 0.10 μ M) and **4d** (R = OH, EC₅₀ = 0.05 μ M) derivatives and 2-naphthyl **7g** (EC₅₀ = 0.45 μ M) derivative as potent P-gp modulating agents.



Synthesis and evaluation of homodimeric GnRHR antagonists having a rigid bis-propargylated benzene core

pp 3744–3758

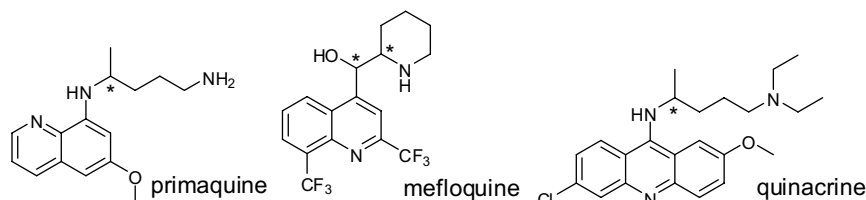
Kimberly M. Bonger, Richard J. B. H. N. van den Berg, Annemiek D. Knijnenburg, Laura H. Heitman, Ad P. IJzerman, Julia Oosterom, Cornelis M. Timmers, Herman S. Overkleeft* and Gijsbert A. van der Marel*



Selective plasma protein binding of antimalarial drugs to α_1 -acid glycoprotein

pp 3759–3772

Ferenc Zsila,* Júlia Visy, György Mády and Ilona Fitos



The acute-phase component serum α_1 -acid glycoprotein is an important contributor in plasma protein binding of antimalarial agents of quinoline and acridine type.

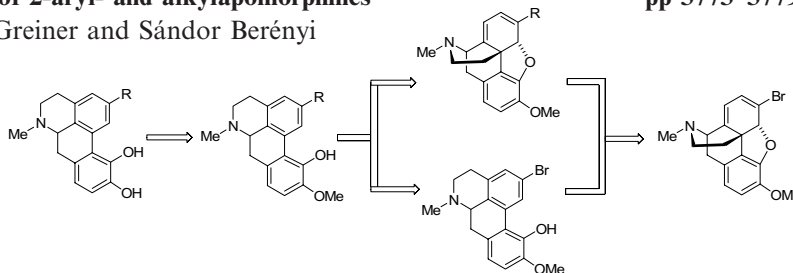


Synthesis and neuropharmacological evaluation of 2-aryl- and alkylapomorphines

pp 3773–3779

Attila Sipos,* Béla Kiss, Éva Schmidt, István Greiner and Sándor Berényi

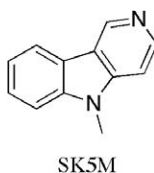
A novel synthesis has been elaborated for the pharmacologically remarkable 2-aryl- and alkylapomorphines described and characterized in the last few years. This new procedure contains two alternative synthetic routes and has allowed the preparation of several hitherto-unknown compounds as well. The pharmacological profile of the previously published and the novel 2-alkyl- and arylapomorphines has been determined with the application of in vitro and in vivo techniques. For 2-phenyl- (2) and 2-(4-hydroxyphenyl)apomorphines (3) the superior dopamine agonist profile has been confirmed and for the novel compounds some remarkable results have been observed.



γ -Carboline derivatives with anti-bovine viral diarrhea virus (BVDV) activity

pp 3780–3790

Kumiko Sako, Hiroshi Aoyama,* Shinichi Sato, Yuichi Hashimoto and Masanori Baba*

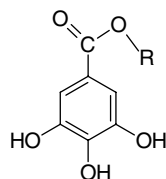


Based on anti-viral screening of our heteroaromatics derived from thalidomide, the γ -carboline skeleton has been identified as a superior scaffold structure for compounds with potent anti-bovine viral diarrhea virus (BVDV) activity. Structural development studies led to a potent anti-viral agent, SK5M (5-methyl- γ -carboline), with the EC_{50} of 0.26 μ M.

Ester derivatives of gallic acid with potential toxicity toward L1210 leukemia cells

pp 3791–3799

Claudriana Locatelli, Rober Rosso, Maria C. Santos-Silva, Camila A. de Souza, Marley A. Licínio, Paulo Leal, Maria L. Bazzo, Rosendo A. Yunes and Tânia B. Creczynski-Pasa*

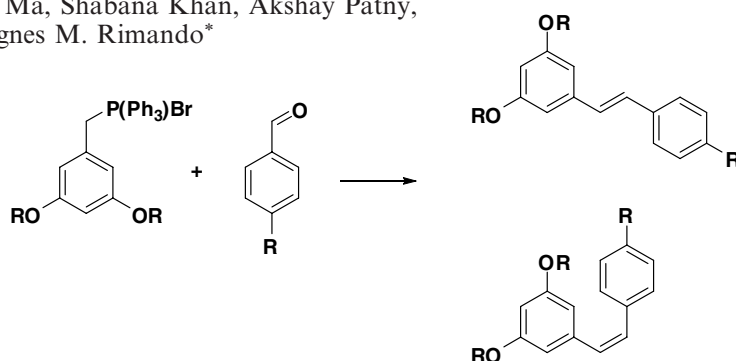


Gallic acid ester derivatives, with the same number of hydroxyl groups, varying the carbon side chain length, induced cell death through apoptosis in a leukemia cell line.

Design, synthesis, biological evaluation and docking studies of pterostilbene analogs inside PPAR α

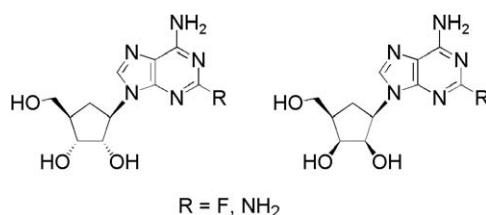
pp 3800–3808

Cassia S. Mizuno, Guoyi Ma, Shabana Khan, Akshay Patny, Mitchell A. Avery and Agnes M. Rimando*

**Synthesis of 2-modified aristeromycins and their analogs as potent inhibitors against *Plasmodium falciparum* S-adenosyl-L-homocysteine hydrolase**

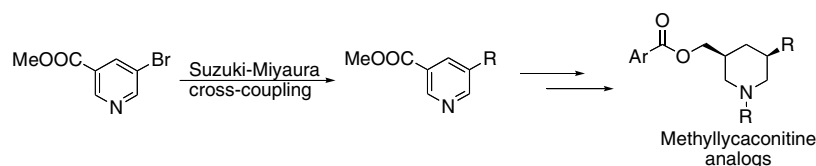
pp 3809–3815

Takayuki Ando, Masafumi Iwata, Fazila Zulfiqar, Tatsuya Miyamoto, Masayuki Nakanishi and Yukio Kitade*

**The synthesis of 5-substituted ring E analogs of methyllycaconitine via the Suzuki–Miyaura cross-coupling reaction**

pp 3816–3824

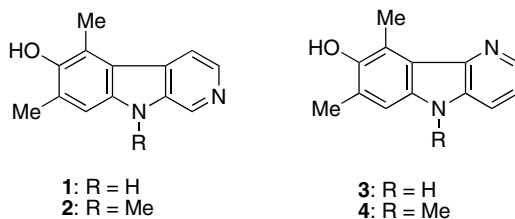
Junfeng Huang, Crina M. Orac, Susan McKay, Dennis B. McKay and Stephen C. Bergmeier*



Synthesis of eudistomin D analogues and its effects on adenosine receptors

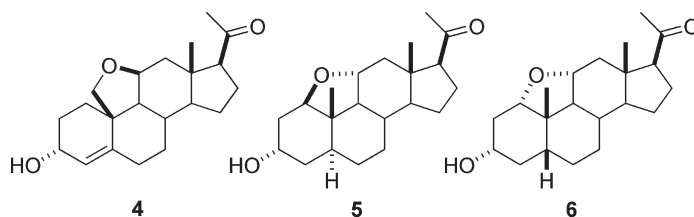
pp 3825–3830

Haruaki Ishiyama, Kengo Ohshita, Tetsuro Abe, Hiroyasu Nakata and Jun'ichi Kobayashi*

**Synthesis and GABA_A receptor activity of oxygen-bridged neurosteroid analogs**

pp 3831–3838

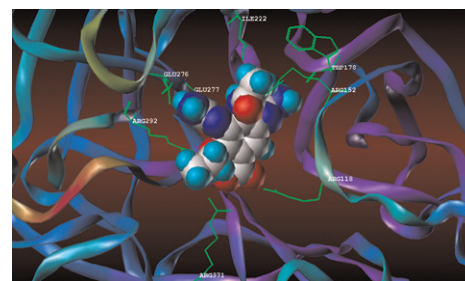
Lautaro D. Alvarez, Adriana S. Veleiro, Ricardo F. Baggio, María T. Garland, Valeria C. Edelsztejn, Héctor Coirini and Gerardo Burton*

**Design, synthesis, inhibitory activity, and SAR studies of hydrophobic *p*-aminosalicylic acid derivatives as neuraminidase inhibitors**

pp 3839–3847

Jie Zhang, Qiang Wang, Hao Fang, Wenfang Xu,* Ailin Liu and Guanhua Du

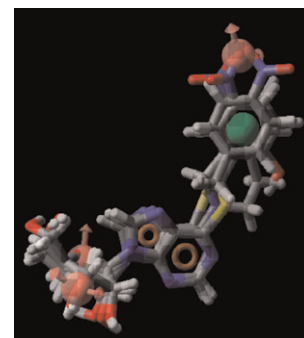
Superposition of compound **12** bound to influenza A (H3N2) neuraminidase. Structure-based design has led to the synthesis of a series of influenza neuraminidase (NA) inhibitors containing benzoic acid. Several compounds exhibit some specific activity against influenza A (H3N2).

**Constrained NBMPR analogue synthesis, pharmacophore mapping and 3D-QSAR modeling of equilibrative nucleoside transporter 1 (ENT1) inhibitory activity**

pp 3848–3865

Zhengxiang Zhu and John K. Buolamwini*

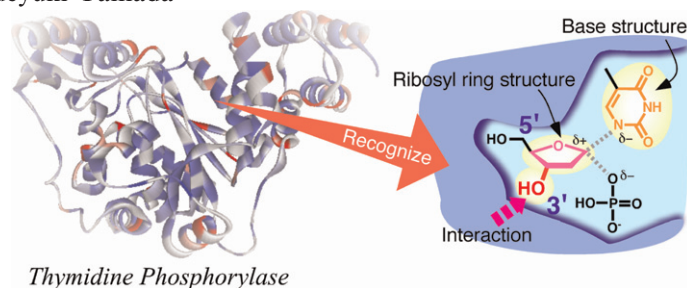
3D Pharmacophore model and suggested bioactive conformation of NBMPR and analogues at their ENT1 transporter-binding site.



Kinetic parameters and recognition of thymidine analogues with varying functional groups by thymidine phosphorylase

pp 3866–3870

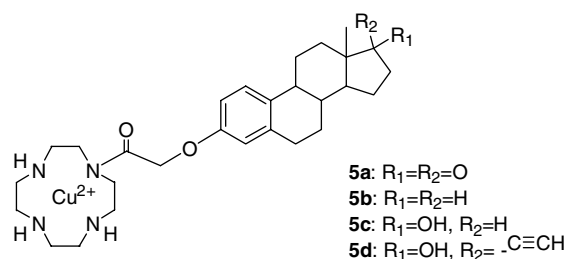
Akihiko Hatano,* Aiko Harano, Yoshikatsu Takigawa, Yasuhiro Naramoto, Keisuke Toda, Yuuichi Nakagomi and Hideyuki Yamada



Synthesis, DNA binding and cleavage activities of the copper (II) complexes of estrogen-macrocyclic polyamine conjugates

pp 3871–3877

Xin-Bin Yang, Jie Feng, Ji Zhang, Zhong-Wei Zhang, Hong-Hui Lin,* Li-Hong Zhou and Xiao-Qi Yu*

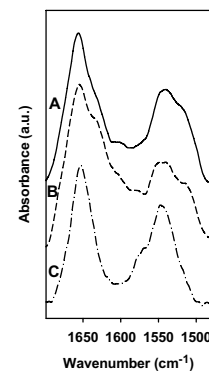


A spectroscopy approach for the study of the interactions of bioactive vanadium species with bovine serum albumin

pp 3878–3886

Evelina G. Ferrer,* Alejandra Bosch, Osvaldo Yantorno and Enrique J. Baran

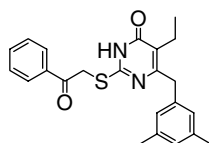
In this article, Fourier transform infrared spectroscopy (FT-IR) and Raman spectroscopy were used to investigate the changes in BSA structure, particularly in its secondary and tertiary structures in the presence of bioactive vanadium species.



Synthesis and biological evaluation of novel 6-substituted 5-alkyl-2-(arylcarbonylmethylthio)pyrimidin-4(3H)-ones as potent non-nucleoside HIV-1 reverse transcriptase inhibitors

pp 3887–3894

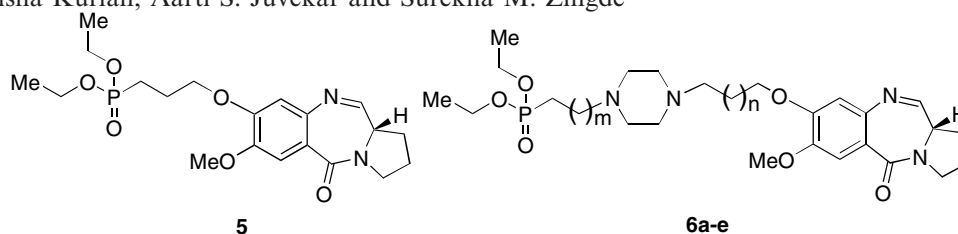
Yue-Ping Wang, Fen-Er Chen,* Erik De Clercq, Jan Balzarini and Christophe Pannecouque



Phosphonate-linked pyrrolo[2,1-c][1,4]benzodiazepine conjugates: Synthesis, DNA-binding affinity and cytotoxicity

pp 3895–3906

Ahmed Kamal,* P. Praveen Kumar, B. N. Seshadri, O. Srinivas, M. Shiva Kumar, Subrata Sen, Nisha Kurian, Aarti S. Juvekar and Surekha M. Zingde



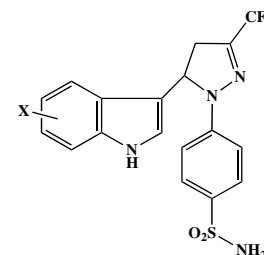
Phosphonate linked pyrrolo[2,1-c][1,4]benzodiazepine conjugates were synthesized and displayed significant anticancer activity against selected human cancer cell lines.

Design, synthesis, and biological evaluation of 1-(4-sulfamylphenyl)-3-trifluoromethyl-5-indolyl pyrazolines as cyclooxygenase-2 (COX-2) and lipoxygenase (LOX) inhibitors

pp 3907–3916

M. V. Ramana Reddy,* Vinay K. Billa, Venkat R. Pallela, Muralidhar R. Mallireddigari, Rengasamy Boominathan, Jerome L. Gabriel and E. Premkumar Reddy*

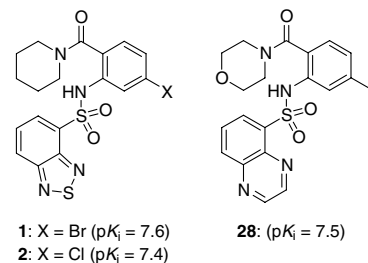
A new series of 1-(4-sulfamylphenyl)-3-trifluoromethyl-5-indolyl pyrazolines were synthesized and evaluated as inhibitors of cyclooxygenase-2 and lipoxygenase-5,12,15 enzymes.


Discovery of potent cholecystokinin-2 receptor antagonists: Elucidation of key pharmacophore elements by X-ray crystallographic and NMR conformational analysis

pp 3917–3925

Mark D. Rosen,* Michael D. Hack, Brett D. Allison, Victor K. Phuong, Craig R. Woods, Magda F. Morton, Clodagh E. Prendergast, Terrance D. Barrett, Carsten Schubert, Lina Li, Xiaodong Wu, Jiejun Wu, Jamie M. Freedman, Nigel P. Shankley and Michael H. Rabinowitz

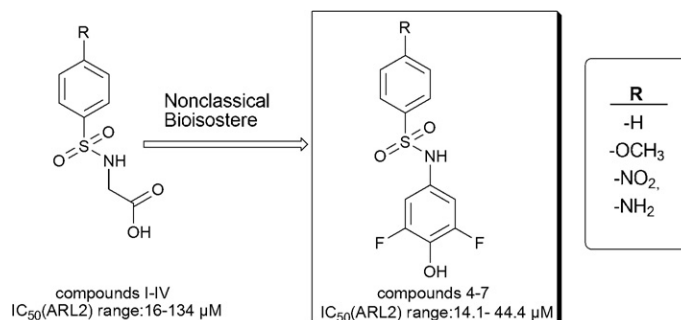
A combination of synthesis, X-ray crystallography, and conformational analysis were used to discover cholecystokinin-2 receptor antagonists with improved pharmacokinetic profiles, and high receptor binding affinity and selectivity.


Design and synthesis of N-(3,5-difluoro-4-hydroxyphenyl)benzenesulfonamides as aldose reductase inhibitors

pp 3926–3932

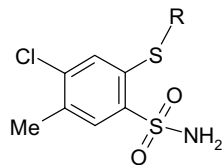
Polyxeni Alexiou, Ioannis Nicolaou, Milan Stefek, Albin Kristl and Vassilis J. Demopoulos*

N-(3,5-Difluoro-4-hydroxyphenyl)benzenesulfonamide (4) and its derivatives 5–7 were designed, synthesized and evaluated for their aldose reductase inhibitory activity. Furthermore, the antioxidant potential as well as the permeability characteristics of 4 was studied.



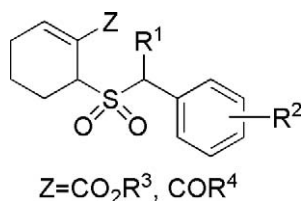
Carbonic anhydrase inhibitors: Inhibition of human cytosolic isozymes I and II and tumor-associated isozymes IX and XII with S-substituted 4-chloro-2-mercapto-5-methyl-benzenesulfonamides pp 3933–3940

Franciszek Sączewski, Alessio Innocenti, Jarosław Sławiński, Anita Kornicka, Zdzisław Brzozowski, Elżbieta Pomarnacka, Andrea Scozzafava, Claudia Temperini and Claudiu T. Supuran*



Novel cyclohexene derivatives as anti-sepsis agents: Synthetic studies and inhibition of NO and cytokine production pp 3941–3958

Masami Yamada,* Takashi Ichikawa, Masayuki Ii, Katsumi Itoh, Norikazu Tamura and Tomoyuki Kitazaki

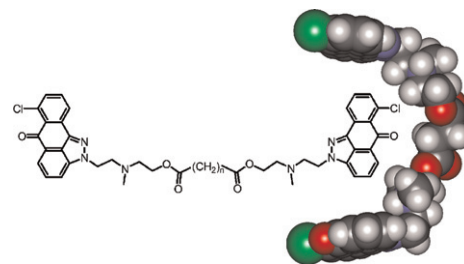


A series of cyclohexane derivatives were synthesized and evaluated for inhibitory activities of NO and cytokine production.

The structure-based design, synthesis and biological evaluation of DNA-binding bisintercalating bisanthrapyrazole anticancer compounds pp 3959–3968

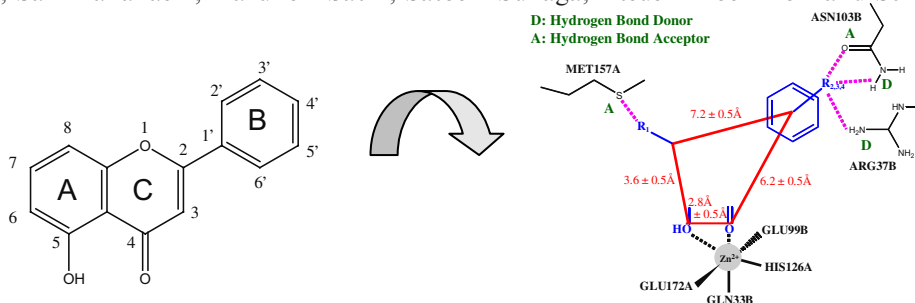
Brian B. Hasinoff,* Hong Liang, Xing Wu, Lynn J. Guziec, Frank S. Guziec, Jr., Kyle Marshall and Jack C. Yalowich

A series of bisanthrapyrazoles with different numbers of methylene linkers selected for their ability to dock into double-stranded DNA were synthesized and physically and biologically evaluated.



Structure–activity relationship of human GLO I inhibitory natural flavonoids and their growth inhibitory effects pp 3969–3975

Ryoko Takasawa, Saki Takahashi, Kazunori Saeki, Satoshi Sunaga, Atsushi Yoshimori and Sei-ichi Tanuma*

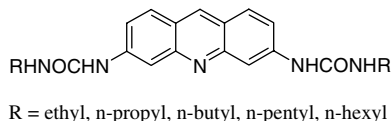


A basic structure of natural flavonoids and their deduced pharmacophore on the human GLO I

Cytotoxic activity of proflavine diureas: Synthesis, antitumor, evaluation and DNA binding properties of 1',1'-(acridin-3,6-diyl)-3',3'-dialkyldiureas

pp 3976–3984

Mária Kožurková, Danica Sabolová, Ladislav Janovec, Jaromír Mikeš, Ján Koval', Ján Ungvarský, Miroslava Štefanišinová, Peter Fedoročko, Pavol Kristian and Ján Imrich*

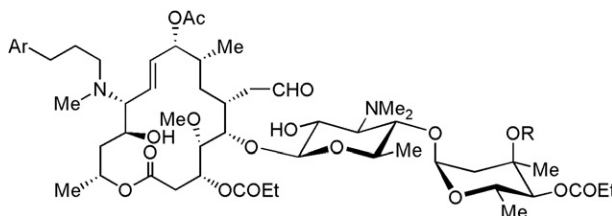


The synthesis of new proflavine derivatives is reported. Drugs were tested against HeLa and HCT-116 cell lines. The binding constants of new compounds with ctDNA have been quantified by spectrofluorimetric titration.

Novel 16-membered macrolides modified at C-12 and C-13 positions of midecamycin A₁ and miokamycin. Part 1: Synthesis and evaluation of 12,13-carbamate and 12-arylalkylamino-13-hydroxy analogues

pp 3985–4002

Tomoaki Miura,* Ken-ichi Kurihara, Takeshi Furuuchi, Takuji Yoshida and Keiichi Ajito*

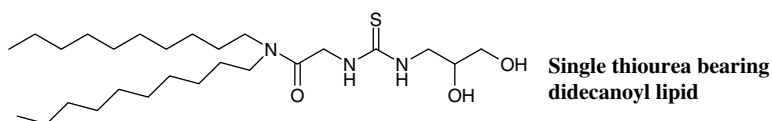


12l: Ar = quinolin-4-yl, R = H
18: Ar = phenyl, R = Ac

A single thiourea group is not enough to get stable thiourea lipoplexes

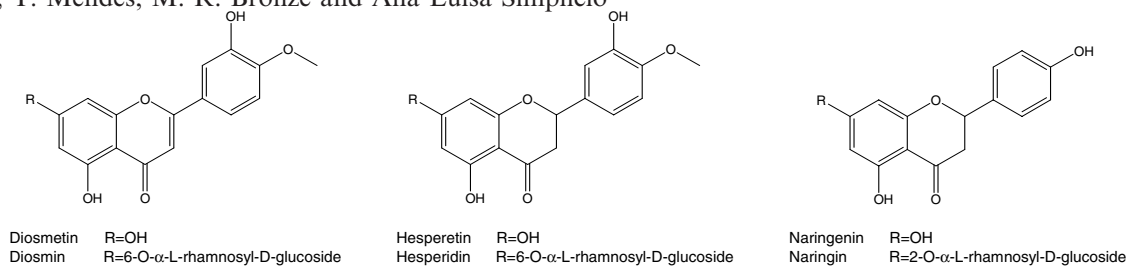
pp 4003–4008

Eihab Kabha, Claire Jacquement, Gaëlle Pembouong, Nathalie Mignet, Daniel Scherman and Jean Herscovici*


Prediction of intestinal absorption and metabolism of pharmacologically active flavones and flavanones

pp 4009–4018

H. Serra, T. Mendes, M. R. Bronze and Ana Luísa Simplicio*



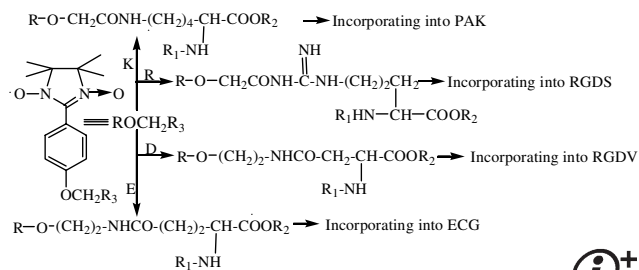
In vitro Caco-2 and PAMPA models were used for assessing permeability of selected flavones and flavanone glycosides and respective aglycones. Ionisation characteristics of these compounds were also evaluated by capillary electrophoresis

A class of novel nitronyl nitroxide labeling basic and acidic amino acids: Synthesis, application for preparing ESR optionally labeling peptides, and bioactivity investigations

pp 4019–4028

Jianwei Zhang, Ming Zhao,* Guohui Cui and Shiqi Peng*

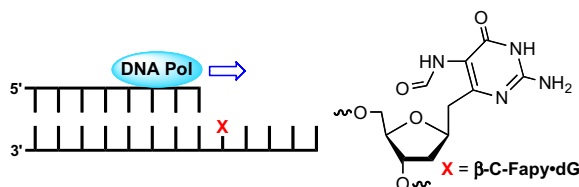
Wherein $R_1 = \text{H, Boc or Z}$; $R_2 = \text{H or CH}_3$; $R_3 = \text{COOH or CH}_2\text{NH}_2$.



DNA polymerase bypass in vitro and in *E. coli* of a C-nucleotide analogue of Fapy-dG

pp 4029–4034

Yvonne N. Weledji, Carissa J. Wiederholt, Michael O. Delaney and Marc M. Greenberg*

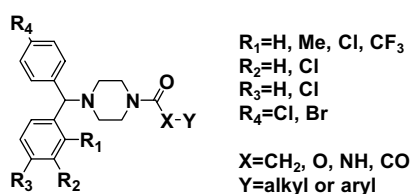


$\beta\text{-C-Fapy-dG}$ is an analogue of Fapy-dG that is stable to repair. DNA polymerase bypass of $\beta\text{-C-Fapy-dG}$ in *Escherichia coli* indicates that it is not mutagenic. $\beta\text{-C-Fapy-dG}$ could be useful as a DNA repair inhibitor.

Design, synthesis and biological evaluation of piperazine analogues as CB1 cannabinoid receptor ligands

pp 4035–4051

Kwang-Seop Song, Sung-Han Lee, Hyun Ji Chun, Jong Yup Kim, Myung Eun Jung, Kwangwoo Ahn, Soo-Un Kim, Jeongmin Kim and Jinhwa Lee*



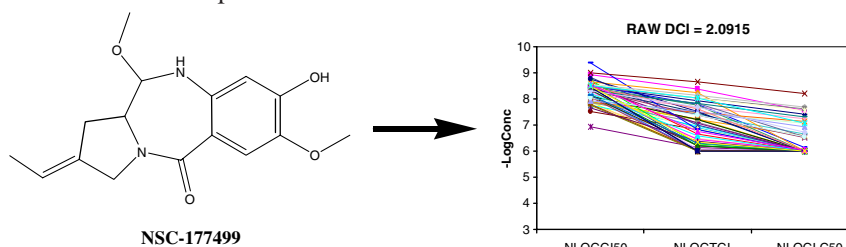
Novel CB1 receptor antagonists were identified, which incorporate piperazine as a central core, and the SAR study was performed. The CB2 binding affinity and the functional profiles were also evaluated.



A structural analysis of the differential cytotoxicity of chemicals in the NCI-60 cancer cell lines

pp 4052–4063

Suman K. Chakravarti* and Gilles Klopman



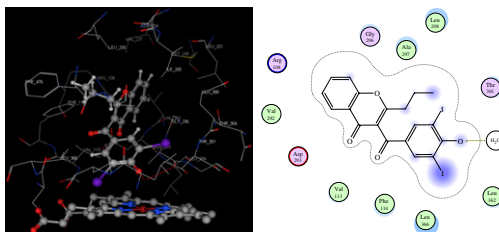
In the present study, molecular structural basis of the differential cytotoxicity of chemicals against NCI-60 cancer cell lines was studied. A number of relevant substructures were identified and predictive models were prepared that can be used to predict differential cytotoxicity of new molecules.



Modeling and synthesis of novel tight-binding inhibitors of cytochrome P450 2C9

pp 4064–4074

Chi-Chi Peng, Tom Rushmore, Gregory J. Crouch and Jeffrey P. Jones*



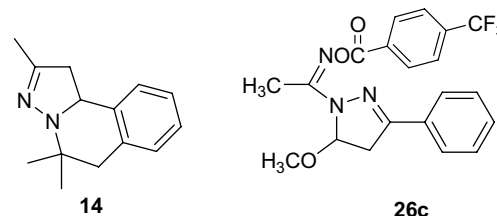
Proposed binding modes of inhibitory analogs would lead to an interaction of the phenolate anion with a water molecule stabilized by Ala 297.

Synthesis, structure and antibacterial activity of novel 1-(5-substituted-3-substituted-4,5-dihydropyrazol-1-yl)ethanone oxime ester derivatives

pp 4075–4082

Xin-Hua Liu,* Pin Cui, Bao-An Song,* Pinaki S. Bhadury, Hai-Liang Zhu and Shi-Fan Wang

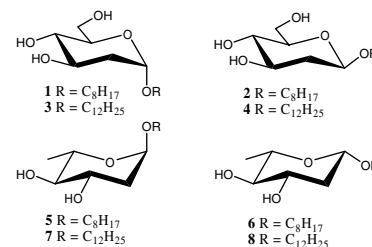
A series of novel 1-(5-substituted-3-substituted-4,5-dihydropyrazol-1-yl)ethanone oxime ester derivatives and the unusual heterocyclic compound 2,5,5-trimethyl-1,5,6,10b-tetrahydropyrazolo[5,1-*a*]isoquinoline are synthesized. The title compounds **14** and **26c** showed potent antibacterial activities against *Staphylococcus aureus* and *Escherichia coli* which was superior to the positive control penicillin.

**Alkyl deoxy-arabino-hexopyranosides: Synthesis, surface properties, and biological activities**

pp 4083–4092

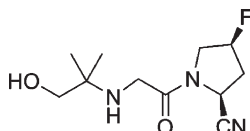
Filipa V. M. Silva, Margarida Goulart, Jorge Justino, Ana Neves, Fernando Santos, João Caio, Susana Lucas, Ana Newton, Diana Sacoto, Ester Barbosa, Maria-Soledade Santos and Amélia P. Rauter*

Synthesis, surface properties, antimicrobial activity, and toxicity.

**Synthesis and structure–activity relationships of potent 4-fluoro-2-cyanopyrrolidine dipeptidyl peptidase IV inhibitors**

pp 4093–4106

Hiroshi Fukushima,* Akira Hiratate, Masato Takahashi, Ayako Mikami, Masako Saito-Hori, Eiji Munetomo, Kiyokazu Kitano, Sumi Chonan, Hidetaka Saito, Akio Suzuki, Yuji Takaoka and Koji Yamamoto

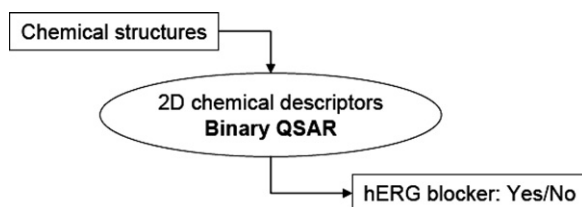


We report the identification of a potent and stable DPP-IV inhibitor (TS-021) with a long-term persistent plasma drug concentration and a potent antihyperglycemic activity.

A binary QSAR model for classification of hERG potassium channel blockers

pp 4107–4119

Khac-Minh Thai and Gerhard F. Ecker*

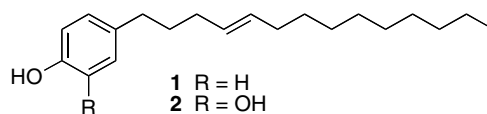


We describe the development and validation of binary QSAR models for rapid classification of hERG potassium channel blockers.

**Bioactive alkenylphenols from *Piper obliquum***

pp 4120–4126

Carola Valdivia, Nieves Marquez, John Eriksson, Antonio Vilaseca, Eduardo Muñoz and Olov Sterner*

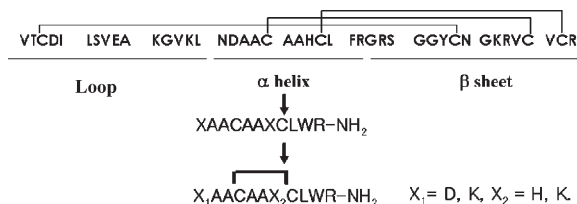


Two new alkenylphenols, obliquol A (1) and obliquol B (2), possessing anti-NF- κ B activity by targeting early events in the TNF α -induced NF- κ B inflammatory pathway, were isolated from *Piper obliquum*.

Design and synthesis of cyclic disulfide-bonded antibacterial peptides on the basis of the α helical domain of Tenecin 1, an insect defensin

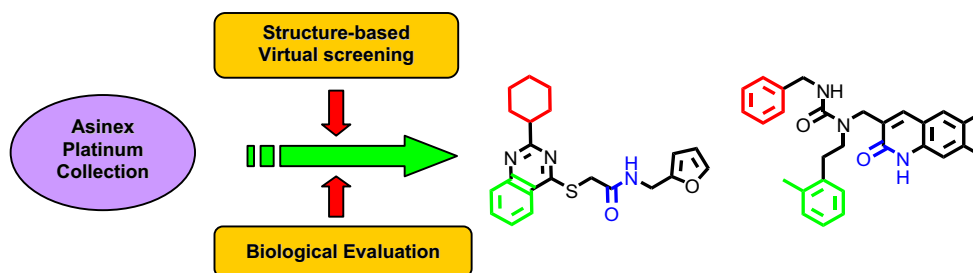
pp 4127–4137

Hye-sun Ahn, Wonmi Cho, Joung-min Kim, Bishnu Prasad Joshi, Jun-won Park, Chuda Raj Lohani, Hyeongjin Cho* and Keun-Hyeung Lee*

**Structure-based virtual screening against SARS-3CL^{pro} to identify novel non-peptidic hits**

pp 4138–4149

Prasenjit Mukherjee, Prashant Desai, Larry Ross, E. Lucile White and Mitchell A. Avery*



Novel inhibitors of the SARS-3CL^{pro} were identified using a combination of structure-based virtual screening and biological evaluation.



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].

Available online at



Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE



ISSN 0968-0896