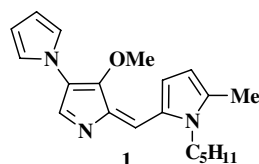


Contents

ARTICLES

A novel naturally occurring tripyrrole with potential nuclease and anti-tumour properties pp 2480–2486

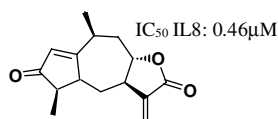
Mahesh Subramanian, Ramesh Chander and Subrata Chattopadhyay*



The natural tripyrrole **1** shows intercalative DNA binding with high G-C specificity and a Cu(II)-dependent nuclease and lipid damaging abilities. The prooxidant activity also assists in its cytotoxicity to tumour cell lines.

Sesquiterpene lactones as inhibitors of IL-8 expression in HeLa cells pp 2487–2497

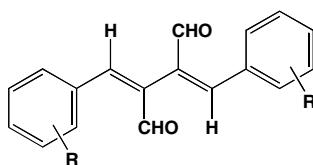
Maja T. Lindenmeyer, Andrea Hrenn, Claudia Kern, Victor Castro, Renato Murillo, Stefan Müller, Stefan Laufer, Jürgen Schulte-Mönting, Bettina Siedle and Irmgard Merfort*



Twenty-four structurally different sesquiterpene lactones were investigated for their inhibitory activity on IL-8 expression and a QSAR study was carried out. Using IC₅₀ values from ELISA experiments an improved correlation factor ($R = 0.821$) was obtained compared to IC₁₀₀ from the NF-κB EMSA ($R = 0.709$). Inhibition of NF-κB as well as AP-1 DNA binding may be involved in downregulation of IL-8 expression.

Synthesis and biological evaluation of dimeric cinnamaldehydes as potent antitumor agents pp 2498–2506

Dae-Seop Shin, Jong-Han Kim, Su-Kyung Lee, Dong Cho Han, Kwang-Hee Son, Hwan-Mook Kim, Hyae-Gyeong Cheon, Kwang-Rok Kim, Nack-Do Sung, Seung Jae Lee, Sung Kwon Kang* and Byoung-Mog Kwon*



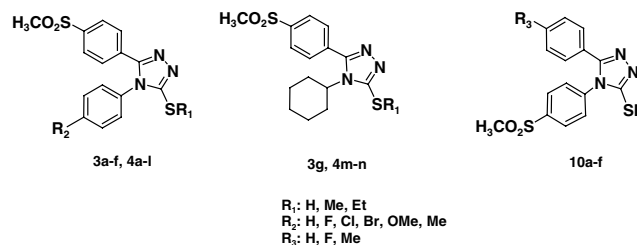
Dimeric cinnamaldehydes (**1–21**) were synthesized based on 2-hydroxycinnamaldehyde. The compounds strongly inhibited the growth of human tumor cells through the inducing apoptosis in tumor cells and in vivo growth of human colon tumor xenograft in nude mice.

Design, synthesis, and biological evaluation of substituted 3-alkylthio-4,5-diaryl-4*H*-1,2,4-triazoles as selective COX-2 inhibitors

pp 2507–2517

Latifeh Navidpour, Hamed Shafaroodi, Khosrou Abdi, Mohsen Amini, Mohammad H. Ghahremani, Ahmad Reza Dehpour and Abbas Shafiee*

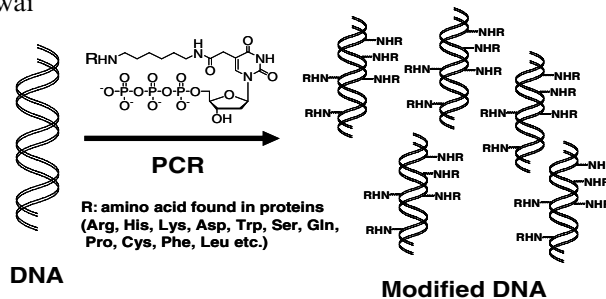
Design, synthesis, and evaluation of a novel class of diaryl-4*H*-1,2,4-triazoles, possessing C-3 thio and alkylthio (SH, SMe or SEt) substituents as selective cyclooxygenase-2 inhibitors (**5a–n**, **11a–f**) are described.



Direct PCR amplification of various modified DNAs having amino acids: Convenient preparation of DNA libraries with high-potential activities for in vitro selection

pp 2518–2526

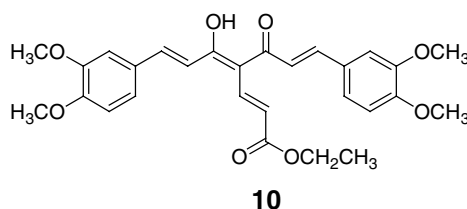
Masayasu Kuwahara, Kazuo Hanawa, Kazuomi Ohsawa, Rina Kitagata, Hiroaki Ozaki and Hiroaki Sawai*



Antitumor agents 247. New 4-ethoxycarbonyl ethyl curcumin analogs as potential antiandrogenic agents

pp 2527–2534

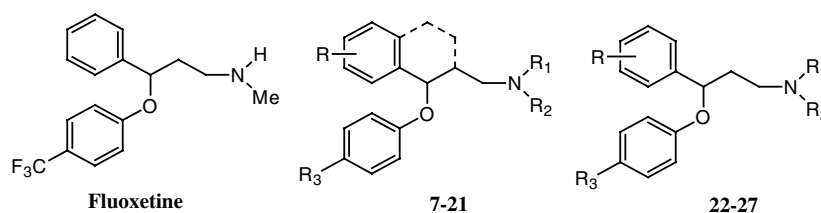
Li Lin, Qian Shi, Ching-Yuan Su, Charles C.-Y. Shih and Kuo-Hsiung Lee*



Synthesis and appetite suppressant activity of 1-aryloxy-2-substituted aminomethyltetrahydronaphthalenes as conformationally rigid analogues of fluoxetine

pp 2535–2544

Kalpna Bhandari,* Shipra Srivastava, Girija Shankar and Chandishwar Nath

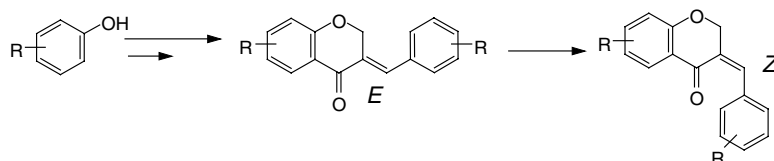


In the present study, synthesis, appetite suppressant activity and SAR of series of new 1-aryloxy-2-substituted aminomethyl tetrahydronaphthalenes (**7–21**) as rigid analogues of fluoxetine and related acyclic compounds (**22–27**) are described.

Synthesis, stereochemical assignments, and biological activities of homoisoflavonoids

pp 2545–2551

Vidavalur Siddaiah, Chunduri Venkata Rao, Somepalli Venkateswarlu,
Alluri V. Krishnaraju and Gottumukkala V. Subbaraju*

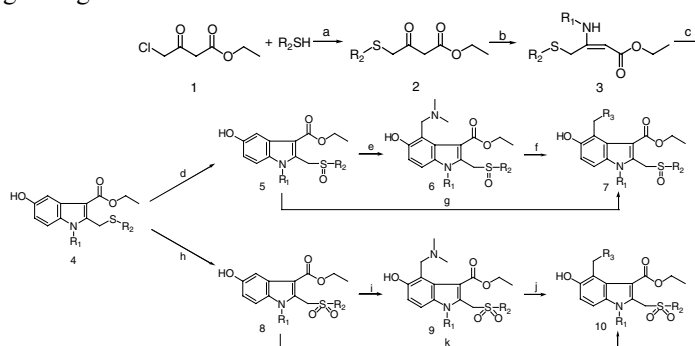


Four naturally occurring homoisoflavonoids and eight analogs were synthesized and evaluated for their antioxidative and 5-LOX inhibitory activities.

Synthesis and in vitro anti-hepatitis B virus activities of some ethyl 5-hydroxy-1*H*-indole-3-carboxylates

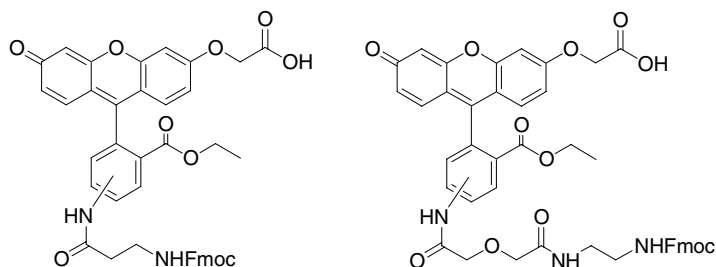
pp 2552–2558

Chunshen Zhao, Yanfang Zhao, Huifang Chai and Ping Gong*

**Fluorescein-based amino acids for solid phase synthesis of fluorogenic protease substrates**

pp 2559–2568

Olga N. Burchak, Laurent Mugherli, François Chatelain and Maxim Y. Balakirev*

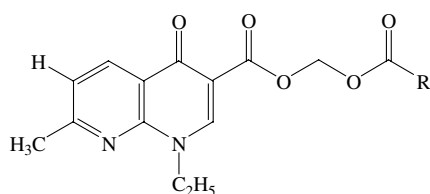


Synthesis, photochemical characterization, and application of new fluorescent amino acids, which can be directly employed in solid phase peptide synthesis, are described.

Efficient approach to acyloxymethyl esters of nalidixic acid and in vitro evaluation as intra-ocular prodrugs

pp 2569–2580

Joëlle Azéma, Brigitte Guidetti, Myriam Malet-Martino,* Robert Martino and Christine Roques



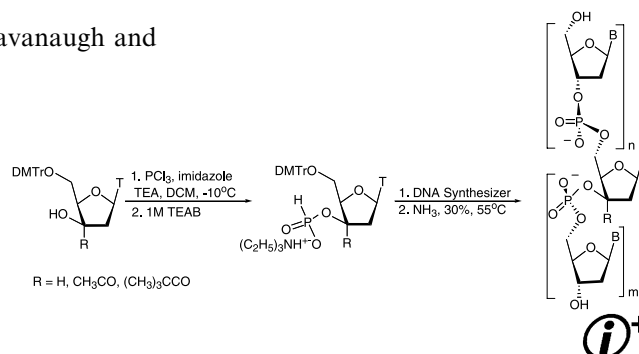
$R = C_nH_{2n+1}$, $n = 3, 7, 11, 13, 15$ or
 $R = C_6H_5-C_7H_{15}$, $C_6H_5-O-C_7H_{15}$

Automated synthesis, characterization, and structural analysis of oligonucleotide C-3'-radical precursors

pp 2581–2588

Georges Lahoud, Jesse Fancher, Sanda Grosu, Breyanna Cavanaugh and Amanda Bryant-Friedrich*

The incorporation of C-3'-acyl-3'-xylothyridine derivatives in oligonucleotides was accomplished using automated *H*-phosphonate methodology. These modified oligomers will be used in the study of oxidative DNA damage processes resulting from the C-3'-radical.



Synthesis and anti-inflammatory activity of a series of N-substituted naproxen glycolamides: Nitric oxide-donor naproxen prodrugs

pp 2589–2599

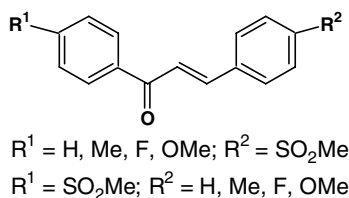
Ramani R. Ranatunge,* Michael E. Augustyniak, Vijay Dhawan, James L. Ellis, David S. Garvey, David R. Janero, L. Gordon Letts, Stewart K. Richardson, Mathew J. Shumway, A. Mark Trocha, Delano V. Young and Irina S. Zemtseva

The synthesis of a series of NO-donating N-substituted glycolamides of naproxen and their anti-inflammatory activity, naproxen release, potential for NO formation, and gastrointestinal safety are reported.

Design, synthesis, and biological evaluation of 1,3-diarylprop-2-en-1-ones: A novel class of cyclooxygenase-2 inhibitors

pp 2600–2605

Afshin Zarghi, Sara Arfaee, P. N. P. Rao and Edward E. Knaus*

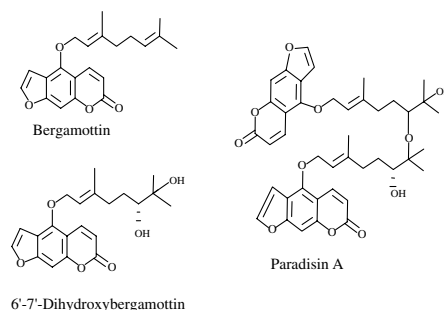


Furocoumarins from grapefruit juice and their effect on human CYP 3A4 and CYP 1B1 isoenzymes

pp 2606–2612

Basavaraj Girennavar, Shibu M. Poullose, Guddadarangavvanahally K. Jayaprakasha, Narayan G. Bhat and Bhimanagouda S. Patil*

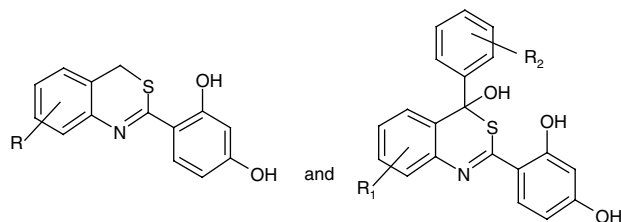
Three furocoumarins were isolated from grapefruit juice. The structures were identified and confirmed by NMR. All three compounds were tested for their inhibitory effects on human CYP 3A4 and CYP 1B1 microsomes using specific substrates such as dibenzylfluorescein and alkoxyresorufin. Paradisin A was found to be the most potent CYP 3A4 inhibitor with an IC_{50} of 1.2 μM followed by DHB and bergamottin. Inhibitory effects on CYP 1B1 exhibited a greater variation due to specificity of substrates. Paradisin A showed an IC_{50} of $3.56 \pm 0.12 \mu\text{M}$ for the ethoxy resorufin *O*-dealkylase activity and $33.56 \pm 0.72 \mu\text{M}$ for the benzyloxyresorufin *O*-dealkylase activity.



Synthesis, antiproliferative and antifungal activities of some 2-(2,4-dihydroxyphenyl)-4*H*-3,1-benzothiazines

pp 2613–2619

Joanna Matysiak

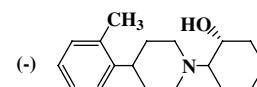


Synthesis and binding affinities of methylvesamicol analogs for the acetylcholine transporter and sigma receptor

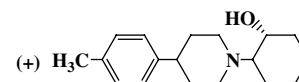
pp 2620–2626

Kazuhiro Shiba,* Kazuma Ogawa, Kiichi Ishiwata, Kazuyoshi Yajima and Hirofumi Mori

Structures of methylvesamicol analogs.



(-)-o-methylvesamicol ((-)-OMV) (13)

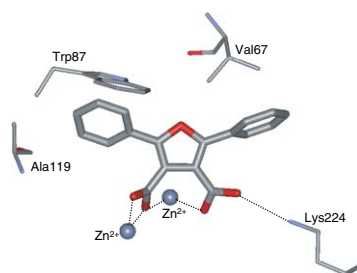


(+)-p-methylvesamicol ((+)-PMV) (16)

New leads of metallo- β -lactamase inhibitors from structure-based pharmacophore design

pp 2627–2635

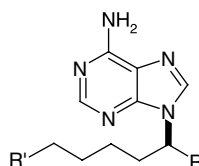
Lars Olsen,* Sandra Jost, Hans-Werner Adolph, Ingrid Pettersson, Lars Hemmingsen and Flemming S. Jørgensen



Binding free energy calculations of adenosine deaminase inhibitors

pp 2636–2641

Alessio Coi, Marco Tonelli, Maria Luisa Ganadu and Anna Maria Bianucci*

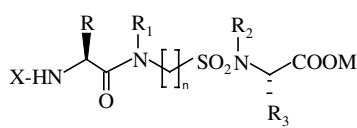


Binding free energy calculations were carried out on a series of inhibitors of adenosine deaminase.

α -Peptide/ β -sulfonamidopeptide hybrids: Analogs of the chemotactic agent for-Met-Leu-Phe-OMe

pp 2642–2652

Cesare Giordano,* Gino Lucente, Annalisa Masi, Mario Paglialunga Paradisi, Anna Sansone and Susanna Spisani

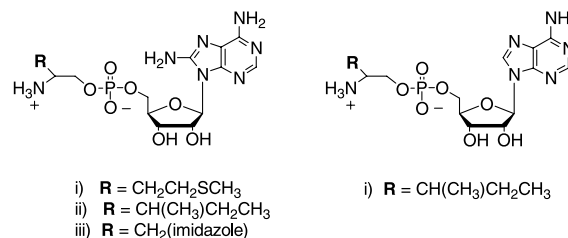
	4/5	R	R ₁	R ₂	R ₃	n
 4a-f) X = Boc 5a-f) X = for	a	CH ₃	H	H	CH ₂ Ph	2
	b	(CH ₂) ₂ SCH ₃	H	H	CH ₃	2
	c	CH ₂ Ph	H	H	(CH ₂) ₂ SCH ₃	2
	d	(CH ₂) ₂ SCH ₃	H	CH ₃	CH ₂ Ph	2
	e	(CH ₂) ₂ SCH ₃	CH ₃	H	CH ₂ Ph	2
	f	(CH ₂) ₂ SCH ₃	H	H	CH ₂ Ph	3

Synthesis of 8-aminoadenosine 5'-(aminoalkyl phosphates), analogues of aminoacyl adenylates

pp 2653–2659

Esmail Yousefi-Salakdeh, Merita Murtola, Anders Zetterberg, Esther Yeheskieli and Roger Strömberg*

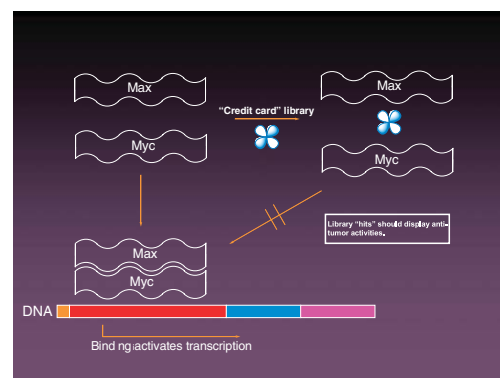
A short and efficient route for the synthesis of aminoalkyl 8-aminoadenylates, potential aminoacyl-tRNA synthetase inhibitors, is presented. Aminoalkyl 8-aminoadenylates were synthesized using a 5'-H-phosphonate strategy involving minimal protecting group manipulations and a single final deprotection step.

**A credit-card library approach for disrupting protein–protein interactions**

pp 2660–2673

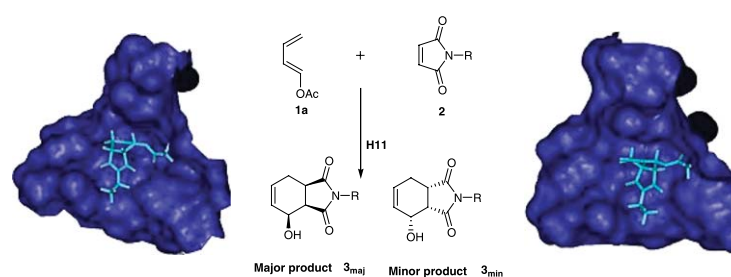
Yang Xu, Jin Shi, Noboru Yamamoto, Jason A. Moss, Peter K. Vogt* and Kim D. Janda*

Protein–protein interfaces are prominent in many therapeutically important targets. Using small organic molecules to disrupt protein–protein interactions is a current challenge in chemical biology. Herein, we report a new strategy for the disruption of protein–protein interactions that has been corroborated through the design and synthesis of a small parallel library termed ‘credit-card’ library. From this 285 membered library, several hits were obtained that disrupted the c-Myc–Max interaction and cellular functions of c-Myc. This strategy for disrupting protein–protein interactions should prove applicable to other families of proteins.

**A modelling study of a non-concerted hydrolytic cycloaddition reaction by the catalytic antibody H11**

pp 2674–2683

Rachel L. Clark, Blair F. Johnston, Colin J. Suckling and Simon P. Mackay*

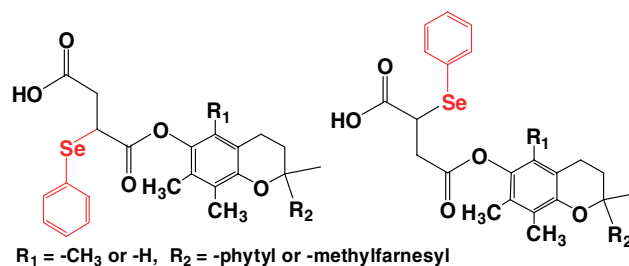


Synthesis and study of the cancer cell growth inhibitory properties of α -, γ -tocopheryl and γ -tocotrienyl 2-phenylselenenyl succinates

pp 2684–2696

Panayiota S. Vraika, Chryssoula Drouza, Maria P. Rikkou, Andreani D. Odysseos* and Anastasios D. Keramidas*

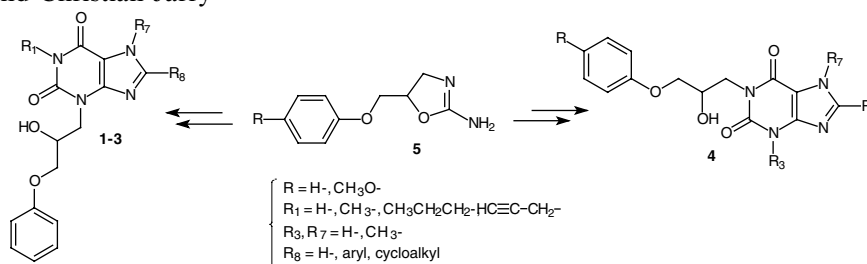
α -Tocopheryl-, γ -tocopheryl-, and γ -tocotrienyl-2-phenylselenenyl succinate were synthesized and characterized by NMR spectroscopy. The vitamin E phenylselenenyl succinate compounds have shown stronger growth inhibitory and pro-apoptotic effect on prostate cancer cell lines than the succinate analogues.



Synthesis and preliminary evaluation of new 1- and 3-[1-(2-hydroxy-3-phenoxypropyl)]xanthines from 2-amino-2-oxazolines as potential A_1 and A_{2A} adenosine receptor antagonists

pp 2697–2719

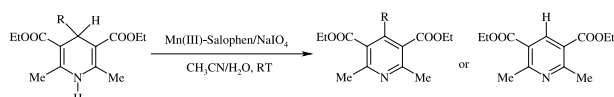
Stéphane Massip, Jean Guillon,* Daniela Bertarelli, Jean-Jacques Bosc, Jean-Michel Léger, Svenja Lacher, Cécile Bontemps, Thibaut Dupont, Christa E. Müller and Christian Jarry



Rapid and efficient oxidation of Hantzsch 1,4-dihydropyridines with sodium periodate catalyzed by manganese (III) Schiff base complexes

pp 2720–2724

Masoud Nasr-Esfahani,* Majid Moghadam,* Shahram Tangestaninejad, Valiollah Mirkhani and Ahmad Reza Momeni

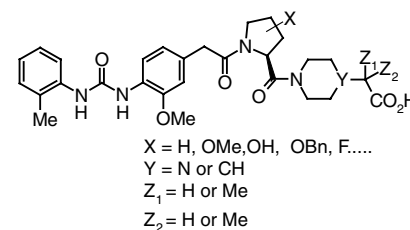


Synthesis, biological evaluation, and pharmacokinetic study of prolyl-1-piperazinylacetic acid and prolyl-4-piperidinylacetic acid derivatives as VLA-4 antagonists

pp 2725–2746

Jun Chiba,* Gensuke Takayama, Tohru Takashi, Mika Yokoyama, Atsushi Nakayama, John J. Baldwin, Edward McDonald, Kevin J. Moriarty, Christopher R. Sarko, Kurt W. Saionz, Robert Swanson, Zahid Hussain, Angela Wong and Nobuo Machinaga

A series of prolyl-1-piperazinylacetic acid and prolyl-4-piperidinylacetic acid derivatives were synthesized and evaluated for their activity as VLA-4 antagonists.

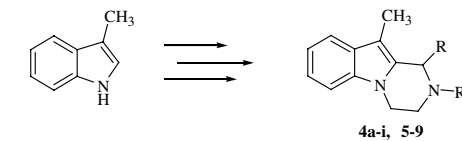


Synthesis and antifungal activity of substituted-10-methyl-1,2,3,4-tetrahydropyrazino[1,2-*a*]indoles

pp 2747–2752

Rakesh Kumar Tiwari, Akhilesh K. Verma,* Anil K. Chhillar, Devender Singh, Jaspal Singh, V. Kasi Sankar, Vibha Yadav, G.L. Sharma and Ramesh Chandra*

Synthesis and antifungal activity studies on substituted-10-methyl-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole derivatives against pathogenic strains of *Aspergilli* and *Candida albicans* reveal that 1-(4-chlorophenyl)-10-methyl-1,2,3,4-tetrahydropyrazino[1,2-*a*]indole **4c** is the most active compound and was found to be less toxic than the standard drug amphotericin B up to the tested concentration, that is, 10,000.0 µg/ml and lysed only 43.75% of human erythrocytes.



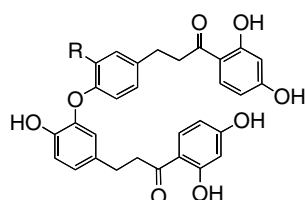
4a-i R¹ = H, R = C₆H₅, *p*-BrC₆H₄, *p*-ClC₆H₄, *p*-FC₆H₄, *p*-MeC₆H₄, *p*-NO₂C₆H₄, *m*-MeOC₆H₄, 2-pyridyl, 2-thienyl, *m*-NO₂C₆H₄

5-9 R = H, R¹ = CH₂Bt, *p*-MeC₆H₄, *n*-C₅H₁₁, *iso*-C₃H₇, CH₃C₂H, CH₂CN, CH₃

Synthesis of verbenachalcone congeners and their biological assessment against activation of the NGF-mediated neurite outgrowth of PC12D cells' activity

pp 2753–2762

Takamasa Tanabe, Takahisa Ogamino, Yoshifumi Shimizu, Masaya Imoto and Shigeru Nishiyama*



R = OMe: Verbenachalcone
R = H: Littorachalcone

Classification of dopamine, serotonin, and dual antagonists by decision trees

pp 2763–2770

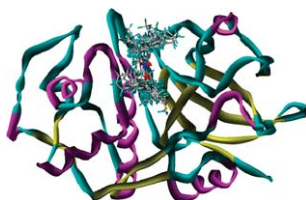
Hye-Jung Kim, Hyunah Choo, Yong Seo Cho, Hun Yeong Koh, Kyoung Tai No and Ae Nim Pae*

Classification model for dopamine antagonists, serotonin antagonist, and serotonin–dopamine dual antagonists was generated using four different classification techniques: LDA (linear discriminant analysis) SIMCA (soft independent modeling of class analogy), RP (recursive partitioning), and ANN (artificial neural networks). The comprehensive structural difference between DA and SA was identified by decisive factors of recursive partitioning trees to design selective antagonist for individual therapy of antipsychotic disorders.

3D-QSAR and docking studies of aldehyde inhibitors of human cathepsin K

pp 2771–2778

Xulin Pan, Ninghua Tan,* Guangzhi Zeng, Hongjin Han and Huoqiang Huang



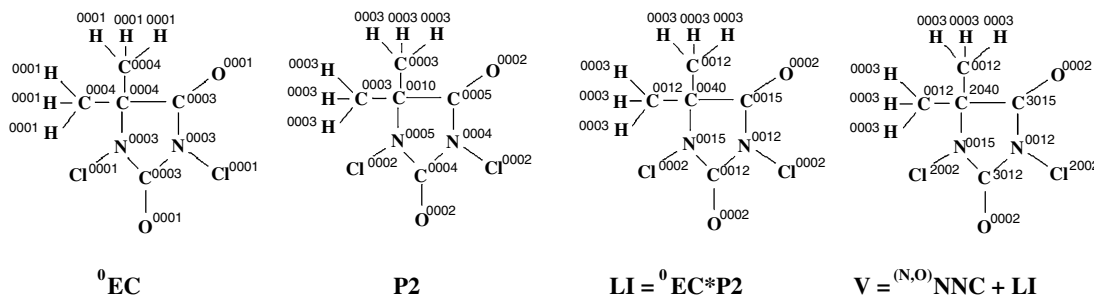
The genetic algorithm of GOLD2.2 has been employed to position 59 aldehyde compounds into the active sites of CatK to determine the probable binding conformation. Based on the docking conformations, highly predictive comparative molecular field analysis (CoMFA) was performed with *q*² value of 0.723.



QSAR models for *Daphnia* toxicity of pesticides based on combinations of topological parameters of molecular structures

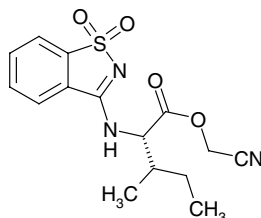
pp 2779–2788

Andrey A. Toropov* and Emilio Benfenati

**Synthesis and in vitro evaluation of pseudosaccharinamine derivatives as potential elastase inhibitors**

pp 2789–2798

Haridas Rode, Stefanie Koerbe, Anita Besch, Karen Methling, Jutta Loose and Hans-Hartwig Otto*

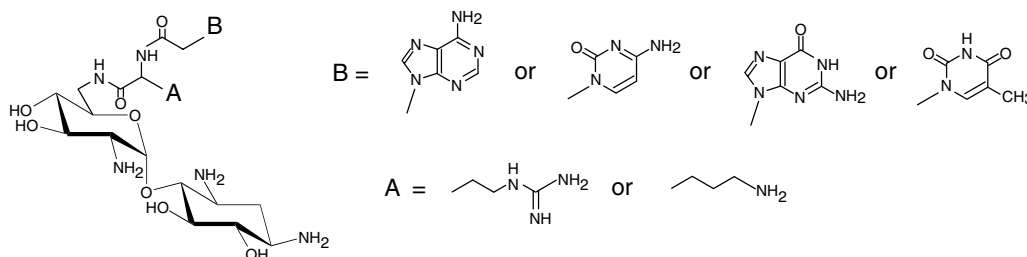


Pseudosaccharinamine derivatives were synthesized and evaluated for inhibitory activity against elastase. $K_i = 0.8 \mu\text{M}$ against HLE

**Neamine derivatives having a nucleobase with a lysine or an arginine as a linker, their synthesis and evaluation as potential inhibitors for HIV TAR–Tat**

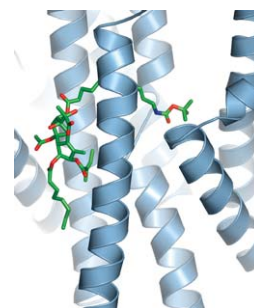
pp 2799–2809

Saki Yajima, Hirohito Shionoya, Takashi Akagi and Keita Hamasaki*

**Natural products as starting materials for development of second-generation SERCA inhibitors targeted towards prostate cancer cells**

pp 2810–2815

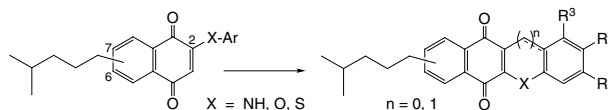
Helmer Søhoel, Anne-Marie Lund Jensen, Jesper V. Møller, Poul Nissen, Samuel R. Denmeade, John T. Isaacs, Carl Erik Olsen and S. Brøgger Christensen*



Synthesis and cytotoxicity of new heterocyclic terpenyl-naphthoquinones

pp 2816–2827

José M. Miguel del Corral,* M^a Angeles Castro, Marina Gordaliza, M^a Luz Martín,
Ana M^a Gamito, Carmen Cuevas and Arturo San Feliciano

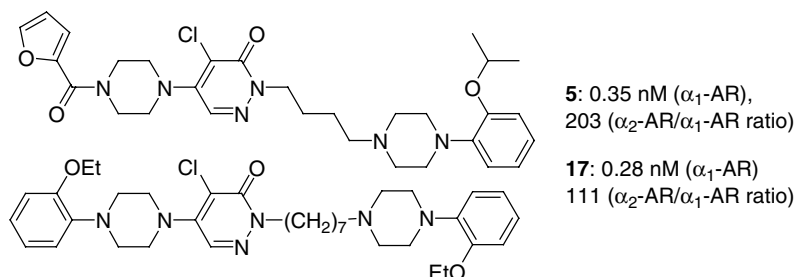


Several heterocyclic terpenyl-naphthoquinones have been prepared by palladium (II)-catalyzed oxidative cyclization of the corresponding substituted naphthoquinones and evaluated as antineoplastics.

Synthesis of new piperazine–pyridazinone derivatives and their binding affinity toward α_1 -, α_2 -adrenergic and 5-HT_{1A} serotonergic receptors

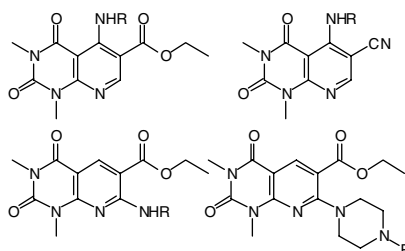
pp 2828–2836

Laura Betti, Marco Zanelli, Gino Giannaccini, Fabrizio Manetti,*
Silvia Schenone and Giovannella Strappaghetti*

**Synthesis and pharmacology of pyrido[2,3-d]pyrimidinediones bearing polar substituents as adenosine receptor antagonists**

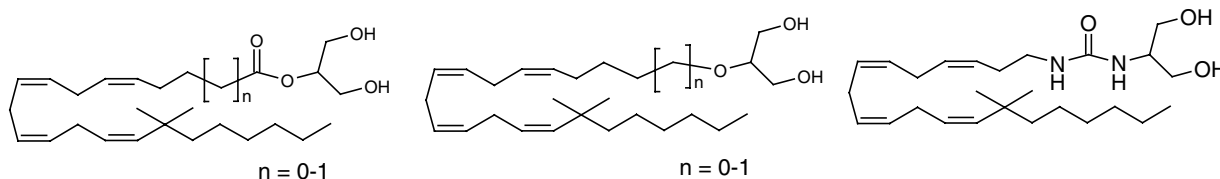
pp 2837–2849

Jacek Bulicz, Daniela C. G. Bertarelli, Dieter Baumert, Friederike Fülle,
Christa E. Müller and Dieter Heber*

**Synthesis and CB1 receptor activities of dimethylheptyl derivatives of 2-arachidonoyl glycerol (2-AG) and 2-arachidonoyl glyceryl ether (2-AGE)**

pp 2850–2858

Teija Parkkari,* Outi M. H. Salo, Kristiina M. Huttunen, Juha R. Savinainen,
Jarmo T. Laitinen, Antti Poso, Tapio Nevalainen and Tomi Järvinen

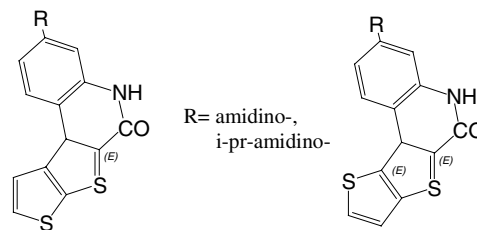


Novel cyano- and amidino-substituted derivatives of thieno[2,3-*b*]- and thieno[3,2-*b*]thiophene-2-carboxanilides and thieno[3',2':4,5]thieno- and thieno[2',3':4,5]thieno [2,3-*c*]quinolones: Synthesis, photochemical synthesis, DNA binding, and antitumor evaluation

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Ivana Jarak, Marijeta Kralj, Ivo Piantanida, Lidija Šuman, Mladen Žinić, Krešimir Pavelić and Grace Karminski-Zamola*

Novel condensed heterocyclic quinolones with amidino substituents were prepared. Their antitumor activity and DNA binding were evaluated.

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Summary of instructions to authors

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i+ 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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ISSN 0968-0896