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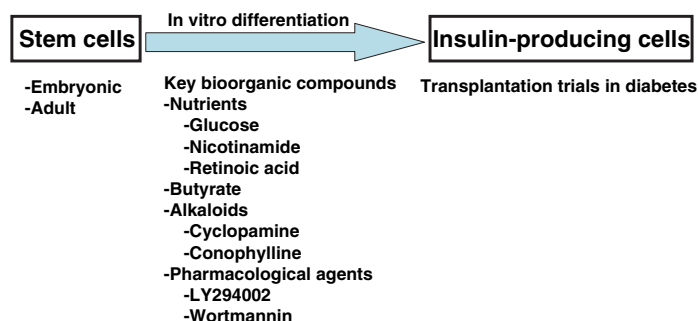
REVIEW

Role of small bioorganic molecules in stem cell differentiation to insulin-producing cells

pp 6466–6474

Enrique Roche,* Jonathan Jones, María Isabel Arribas,
Trinidad Leon-Quinto and Bernat Soria

Stem cells have proven to be of great interest for diabetes treatment. This pathology is caused by β -cell destruction. Obtaining insulin-secreting β -cells from stem cells to implant in diabetic patients is a therapeutic alternative to consider. Bioorganic compounds can help in the control of in vitro differentiation processes towards β -cell-like fates.

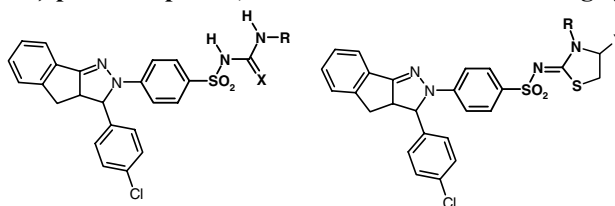


ARTICLES

Synthesis and in vitro antitumor evaluation of some indeno[1,2-*c*]pyrazol(in)es substituted with sulfonamide, sulfonylurea(-thiourea) pharmacophores, and some derived thiazole ring systems

pp 6475–6485

Sherif A. F. Rostom*



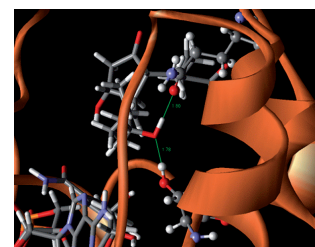
A series of 3-(4-chlorophenyl)-[1,2-*c*]pyrazol(in)es-substituted with benzenesulfonamides, N¹,N³-disubstituted sulfonylurea and sulfonylthiourea pharmacophores, and some derived thiazolidinone and thiazoline ring systems and evaluated for their antitumor activity according to the protocol of the NCI. Eight compounds showed promising broad spectrum antitumor activity against most of the tested subpanel tumor cell lines.

Role of glutamine 148 of human 15-hydroxyprostaglandin dehydrogenase in catalytic oxidation of prostaglandin E₂

pp 6486–6491

Hoon Cho, Lingyu Huang, Adel Hamza, Daquan Gao, Chang-Guo Zhan* and Hsin-Hsiung Tai*

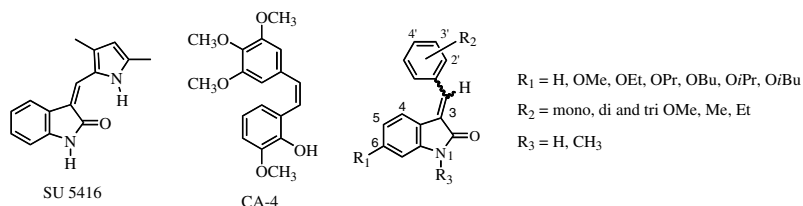
Gln-148 of human 15-hydroxyprostaglandin dehydrogenase is important in the proper positioning of the C-15 hydroxyl group of the prostaglandin E₂ during catalytic oxidation of the substrate. The model indicates that the 15-hydroxyl group of the prostaglandin E₂ is anchored by hydrogen bonding with the hydroxyl group of Ser-138 and the side chain oxygen atom of Gln-148.



Structure–activity-relationship studies of conformationally restricted analogs of combretastatin A-4 derived from SU5416

pp 6492–6501

Bulbul Pandit, Yanjun Sun, Ping Chen, Dan L. Sackett, Zhigen Hu, Wendy Rich, Chenglong Li, Andrew Lewis, Kevin Schaefer and Pui-Kai Li*

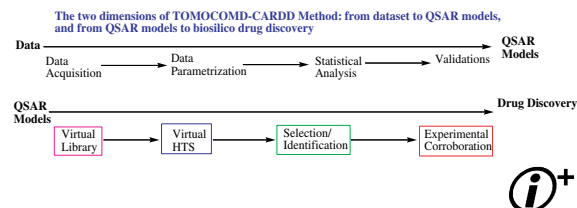


Predicting antitrichomonal activity: A computational screening using atom-based bilinear indices and experimental proofs

pp 6502–6524

Yovani Marrero-Ponce,* Alfredo Meneses-Marcel, Juan A. Castillo-Garit, Yanetsy Machado-Tugores, José Antonio Escario, Alicia Gómez Barrio, David Montero Pereira, Juan José Nogal-Ruiz, Vicente J. Arán, Antonio R. Martínez-Fernández, Francisco Torrens, Richard Rotondo, Froylán Ibarra-Velarde and Ysaías J. Alvarado

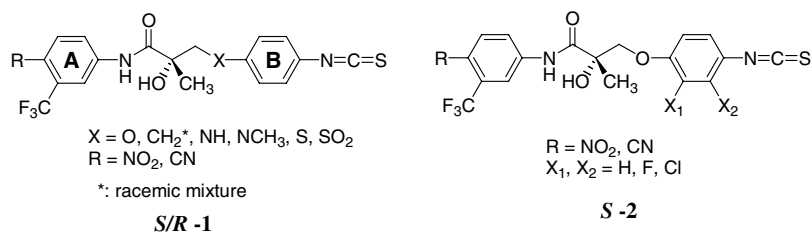
The two dimensions of TOMOCOMD-CARDD method: from dataset to QSAR models, and from QSAR models to biosilico drug discovery.



Arylthiocyanato selective androgen receptor modulators (SARMs) for prostate cancer

pp 6525–6538

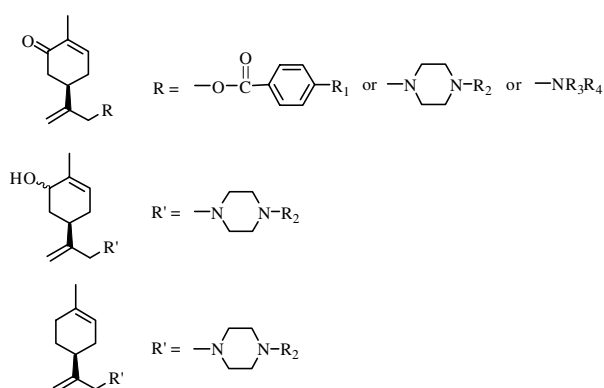
Dong Jin Hwang, Jun Yang, Huiping Xu, Igor M. Rakov, Michael L. Mohler, James T. Dalton and Duane D. Miller*



The synthesis of L-carvone and limonene derivatives with increased antiproliferative effect and activation of ERK pathway in prostate cancer cells

pp 6539–6547

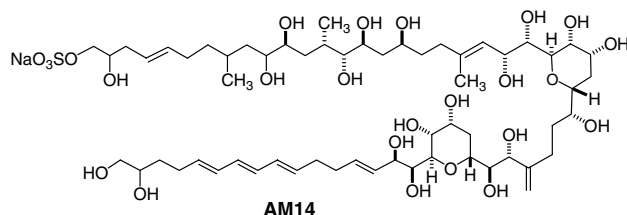
Jiaojiao Chen, Min Lu, Yongkui Jing* and Jinhua Dong*



Structures of new amphidinols with truncated polyhydroxyl chain and their membrane-permeabilizing activities

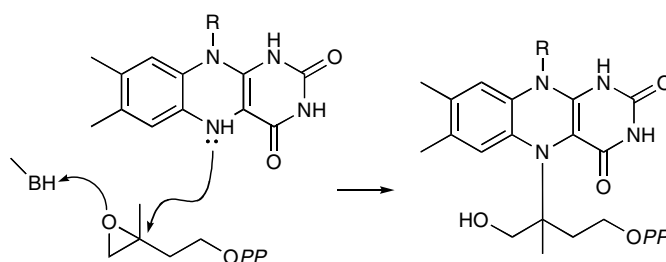
pp 6548–6554

Nagy Morsy, Toshihiro Houdai, Shigeru Matsuoka, Nobuaki Matsumori, Seiji Adachi, Tohru Oishi, Michio Murata,* Takashi Iwashita and Tsuyoshi Fujita

**Inhibition of type 2 isopentenyl diphosphate isomerase from *Methanocaldococcus jannaschii* by a mechanism-based inhibitor of type 1 isopentenyl diphosphate isomerase**

pp 6555–6559

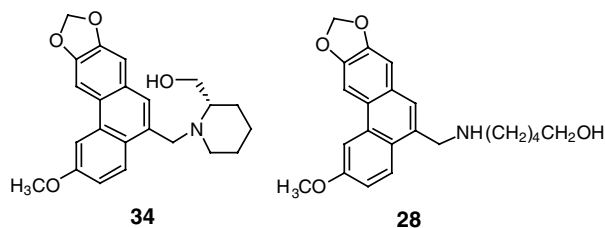
Takeshi Hoshino, Hideyuki Tamegai, Katsumi Kakinuma and Tadashi Eguchi*

**Antitumor agents 251: Synthesis, cytotoxic evaluation, and structure–activity relationship studies of phenanthrene-based tylophorine derivatives (PBTs) as a new class of antitumor agents**

pp 6560–6569

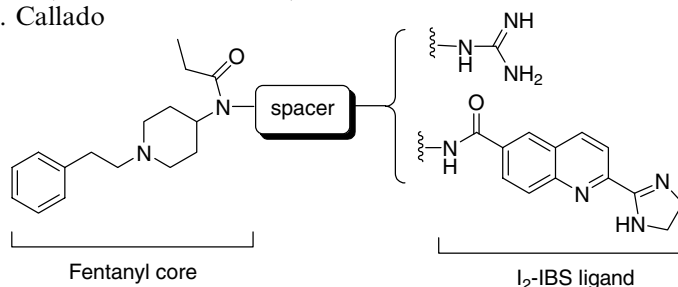
Linyi Wei, Arnold Brossi, Ross Kendall, Kenneth F. Bastow, Susan L. Morris-Natschke, Qian Shi and Kuo-Hsiung Lee*

In a series of polar phenanthrene-based tylophorine derivatives (PBTs), *N*-(2,3-methylenedioxy-6-methoxy-phenanthr-9-ylmethyl)-*L*-2-piperidinemethanol (**34**) and *N*-(2,3-methylenedioxy-6-methoxy-phenanthr-9-ylmethyl)-5-aminopentanol (**28**) showed the highest potency with IC₅₀ values of 0.16 and 0.27 μM, respectively, against the A549 human cancer cell line, which are comparable to those of currently used antitumor drugs.

**Synthesis and pharmacological studies of new hybrid derivatives of fentanyl active at the μ-opioid receptor and I₂-imidazoline binding sites**

pp 6570–6580

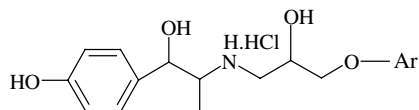
Christophe Dardonville,* Cristina Fernandez-Fernandez, Sarah-Louise Gibbons, Gary J. Ryan, Nadine Jagerovic, Ane M. Gabilondo, J. Javier Meana and Luis F. Callado



Synthesis and evaluation of uterine relaxant activity for a novel series of substituted *p*-hydroxyphenylethanolamines

pp 6581–6585

C. L. Viswanathan* and A. S. Chaudhari

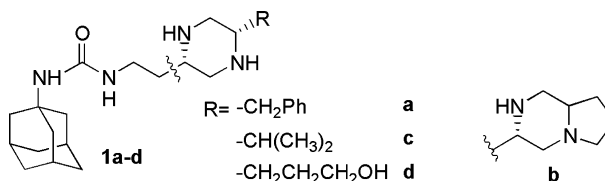


Synthesis and evaluation of 1-(4-hydroxyphenyl)-2-[3-(substituted phenoxy)-2-hydroxy-1-propyl]aminopropan-1-ol hydrochlorides as uterine relaxants is reported.

The 5-substituted piperazine as a novel secondary pharmacophore greatly improving the physical properties of urea-based inhibitors of soluble epoxide hydrolase

pp 6586–6592

Hui-Yuan Li, Yi Jin, Christophe Morisseau, Bruce D. Hammock and Ya-Qiu Long*



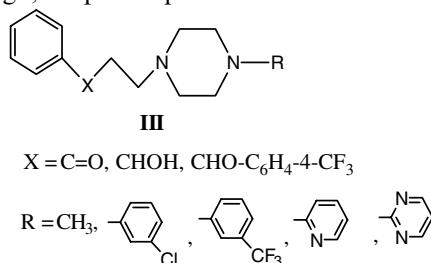
A new class of sEH inhibitors was designed and synthesized by the incorporation of 5-substituted piperazine as a favorable secondary pharmacophore into 1,3-dialkyl urea platform, with greatly improved physical properties.



Synthesis of benzenepropanamine analogues as non-detergent spermicides with antitrichomonas and anticandida activities

pp 6593–6600

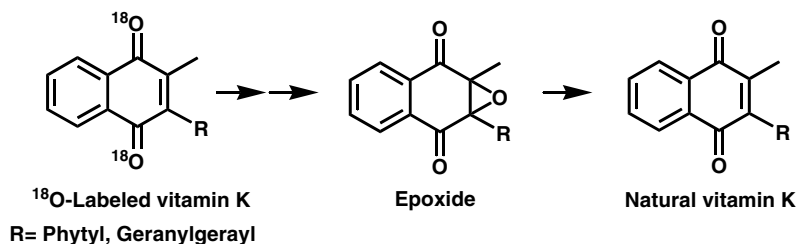
S. T. V. S. Kiran Kumar, Vishnu Lal Sharma,* Manish Kumar, Praveen Kumar Shukla, Pratibha Tiwari, Rajeev Kumar Jain, Jagdamba Prasad Maikhuri, Divya Singh, Gopal Gupta and Man Mohan Singh



Comparative uptake, metabolism, and utilization of menaquinone-4 and phyloquinone in human cultured cell lines

pp 6601–6607

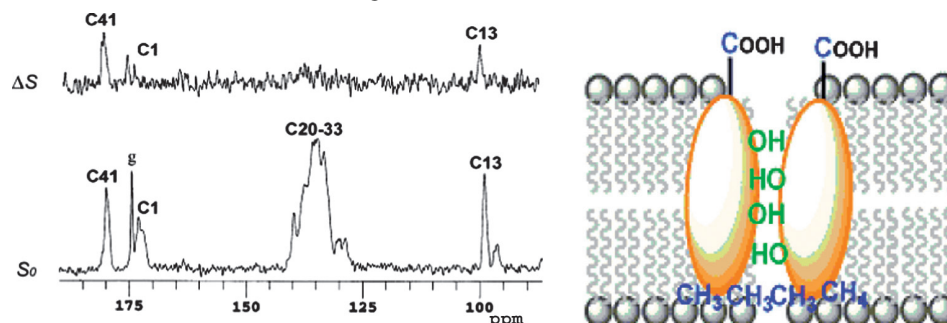
Yoshitomo Suhara, Aya Murakami, Kimie Nakagawa, Yukari Mizuguchi and Toshio Okano*



Membrane interaction of amphotericin B as single-length assembly examined by solid state NMR for uniformly ^{13}C -enriched agent

pp 6608–6614

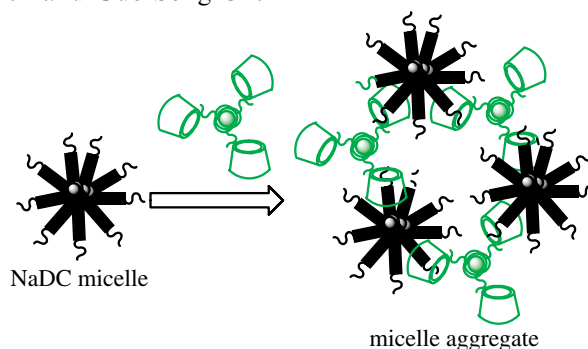
Shigeru Matsuoka, Hiroki Ikeuchi, Yuichi Umegawa, Nobuaki Matsumori and Michio Murata*



Secondary assembly of bile salts mediated by β -cyclodextrin–terbium(III) complex

pp 6615–6620

Yu Liu,* Ning Zhang, Yong Chen and Guo-Song Chen

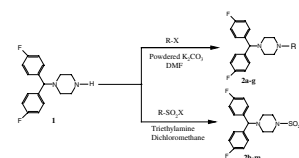


Synthesis and in vitro antimicrobial studies of medicinally important novel *N*-alkyl and *N*-sulfonyl derivatives of 1-[bis(4-fluorophenyl)-methyl]piperazine

pp 6621–6627

J. N. Narendra Sharath Chandra, C. T. Sadashiva, C. V. Kavitha and K. S. Rangappa*

A series of novel substituted 1-[bis(4-fluorophenyl)-methyl]piperazine derivatives (**2a–m**) have been synthesized. The synthesized compounds were characterized by IR and ^1H NMR. All the synthesized compounds were evaluated in vitro for their efficacy as antimicrobial agents against representative strains of Gram-positive (*Staphylococcus aureus* ATCC 25953, *Streptococcus pneumoniae* ATCC 49619, *Bacillus cereus* 11778, and *Bacillus subtilis* 6051) and Gram-negative bacteria (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 2853, *Proteus vulgaris* ATCC 2853, and *Salmonella typhi* ATCC 9484) by paper disc diffusion and microdilution methods. Among the newly synthesized compounds **2e**, **2l**, and **2m** showed potent antimicrobial activities, when compared to the standard drug.



Discovery of heteroaryl sulfonamides as new EP1 receptor selective antagonists

pp 6628–6639

Atsushi Naganawa,* Toshiaki Matsui, Tetsuji Saito, Masaki Ima, Tadashi Tatsumi, Shingo Yamamoto, Masayuki Murota, Hiroshi Yamamoto, Takayuki Maruyama, Shuichi Ohuchida, Hisao Nakai, Kigen Kondo and Masaaki Toda

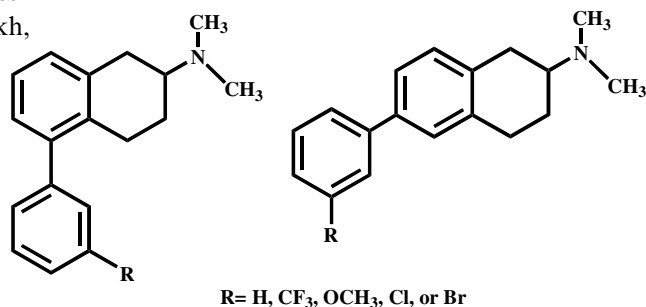
	Ar	1	2	3 Me	4
	EP1 function (IC_{50} , μM)	0.13	0.0039	0.0022	0.006
	clogP	6.91	5.56	6.08	5.47

Heteroaryl sulfonamide derivatives **2–4** were identified as more potent and less lipophilic EP1 receptor antagonists than **1**.

Novel ligands for the human histamine H₁ receptor: Synthesis, pharmacology, and comparative molecular field analysis studies of 2-dimethylamino-5-(6)-phenyl-1,2,3,4-tetrahydronaphthalenes

pp 6640–6658

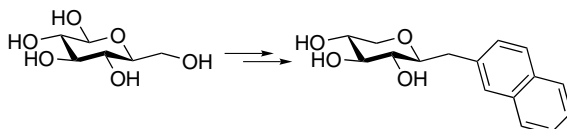
Ola M. Ghoneim, Jacqueline A. Legere, Alexander Golbraikh, Alexander Tropsha and Raymond G. Booth*



Synthesis of aromatic C-xylosides by position inversion of glucose

pp 6659–6665

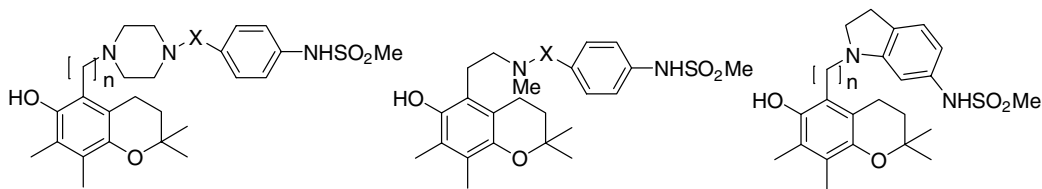
Jesper Malmberg, Katrin Mani, Elin Säwén, Anders Wirén and Ulf Ellervik*



Synthesis and biological evaluation of benzopyran analogues bearing class III antiarrhythmic pharmacophores

pp 6666–6678

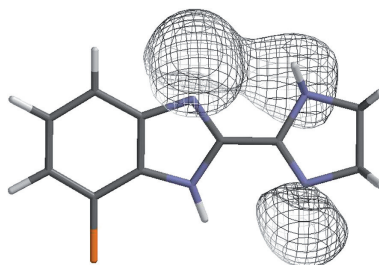
Maria Koufaki,* Christina Kiziridi, Panagiota Papazafiri, Athanasios Vassilopoulos, Andr s Varr , Zsolt Nagy, Attila Farkas and Alexandros Makriyannis



2-(4,5-Dihydroimidazol-2-yl)benzimidazoles as highly selective imidazoline I₂/adrenergic  ₂ receptor ligands

pp 6679–6685

Francieszek S czewski,* Piotr Tabin, Robin J. Tyacke, Alys Maconie, Jaros aw S czewski, Anita Kornicka, David J. Nutt and Alan L. Hudson

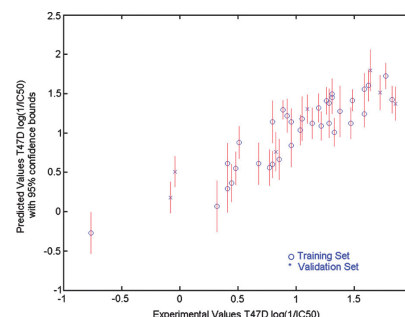


A novel QSAR model for predicting induction of apoptosis by 4-aryl-4H-chromenes

pp 6686–6694

Antreas Afantitis, Georgia Melagraki, Haralambos Sarimveis,* Panayiotis A. Koutentis, John Markopoulos and Olga Iglessi-Markopoulou

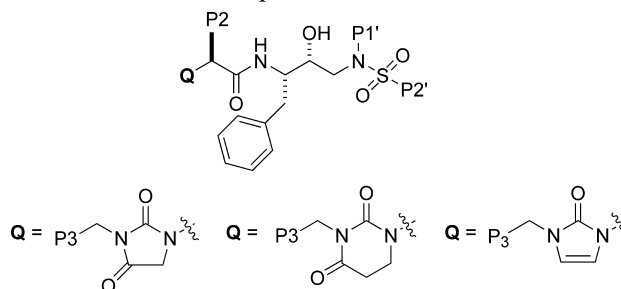
A linear quantitative structure–activity relationship (QSAR) model is presented for modeling and predicting induction of apoptosis by 4-aryl-4H-chromenes. The model was produced by using the multiple linear regression (MLR) technique on a database that consists of 43 recently discovered 4-aryl-4H-chromenes. Among the 61 different physicochemical, topological, and structural descriptors that were considered as inputs to the model, seven variables were selected using the elimination selection-stepwise regression method (ES-SWR). The physical meaning of each descriptor is discussed. The accuracy of the proposed MLR model is illustrated using the following evaluation techniques: cross-validation, validation through an external test set, and Y-randomization. Furthermore, the domain of applicability which indicates the area of reliable predictions is defined.

**Discovery of imidazolidine-2,4-dione-linked HIV protease inhibitors with activity against lopinavir-resistant mutant HIV**

pp 6695–6712

William J. Flosi,* David A. DeGoey, David J. Grampovnik, Hui-ju Chen, Larry L. Klein, Tatyana Dekhtyar, Sherie Masse, Kennan C. Marsh, Hong Mei Mo and Dale Kempf

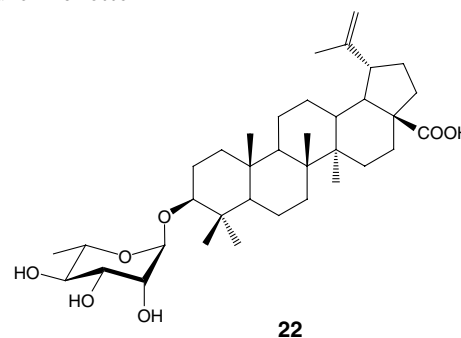
A series of HIV protease inhibitors containing various cyclic structural motifs (**Q**) which occupy subsite S_2 of HIV protease and facilitate the access of P3 groups into subsite S_3 via a *N*-methylene linker was designed and evaluated for their antiviral activity against wild-type HIV virus with and without human serum. Promising compounds were further screened against resistant strains of HIV. In addition, the pharmacokinetic properties in rats were studied.

**Glycosidation of lupane-type triterpenoids as potent in vitro cytotoxic agents**

pp 6713–6725

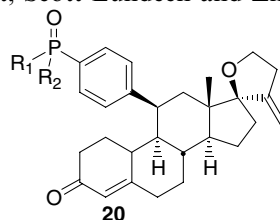
Charles Gauthier, Jean Legault, Maxime Lebrun, Philippe Dufour and André Pichette*

α -L-Rhamnopyranoside of betulinic acid (**22**) exerted the strongest in vitro cytotoxicity of tested glycosides with an activity of 8- to 12-fold more potent toward cancerous cells than on healthy cells.

**New progesterone receptor antagonists: Phosphorus-containing 11 β -aryl-substituted steroids**

pp 6726–6732

Weiqin Jiang,* George Allan, James J. Fiordeliso, Olivia Linton, Pamela Tannenbaum, Jun Xu, Peifang Zhu, Joseph Gunnet, Keith Demarest, Scott Lundeen and Zhihua Sui

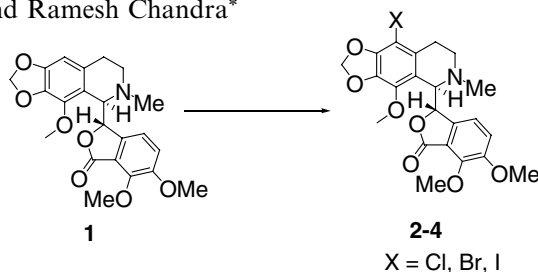


A series of phosphorus-containing 11 β -aryl-substituted steroids were synthesized and evaluated for their in vitro progesterone receptor and glucocorticoid receptor antagonist activities. Selected compounds were tested in rat in C3 assay for PR antagonist activities.

Synthesis and in vitro cytotoxicity of haloderivatives of noscapine

pp 6733–6736

Akhilesh Kumar Verma,* Sandhya Bansal, Jaspal Singh, Rakesh Kumar Tiwari, V. Kasi Sankar, Vibha Tandon and Ramesh Chandra*



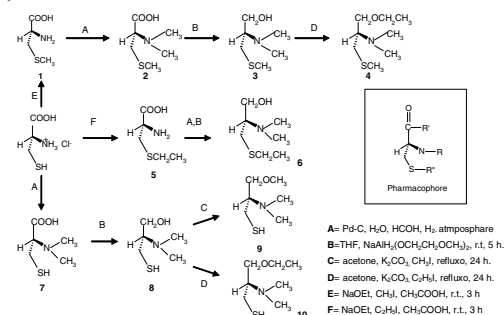
Haloderivatives of noscapine **2–4** were synthesized chemoselectively and their in vitro cytotoxicity was assessed by MTT assay on U-87 human glioblastoma cell lines. 9-Chloronoscapine **2** was found to be more cytotoxic agent than EM011 at 50 μM concentration.

Cysteine based novel noncompetitive inhibitors of urease(s)—Distinctive inhibition susceptibility of microbial and plant ureases

pp 6737–6744

Zareen Amtul,* Naheed Kausar, Cristian Follmer, Richard F. Rozmahel, Atta-Ur-Rahman, Syed Arif Kazmi, Mohammed Saleh Shekhani, Jason L. Eriksen, Khalid M. Khan and Mohammad Iqbal Choudhary*

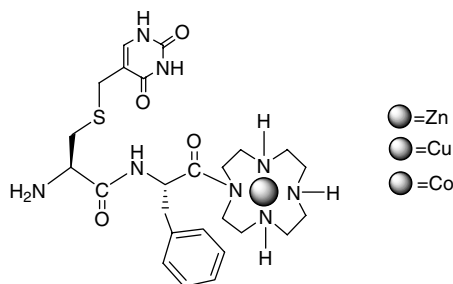
Based on the catalysis mechanism of urease, a homologous series of 10 cysteine derivatives (CysDs) was synthesized, and their inhibitory activities were evaluated for microbial and plant ureases.



Synthesis and DNA cleavage activities of mononuclear macrocyclic polyamine zinc(II), copper(II), cobalt(II) complexes which linked with uracil

pp 6745–6751

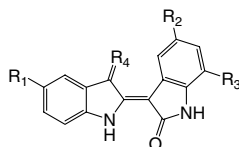
Xiao-Yan Wang, Ji Zhang, Kun Li, Ning Jiang, Shan-Yong Chen, Hong-Hui Lin,* Yu Huang, Li-Jian Ma and Xiao-Qi Yu*



Enhancing effect of indirubin derivatives on 1,25-dihydroxyvitamin D₃- and all-*trans* retinoic acid-induced differentiation of HL-60 leukemia cells

pp 6752–6758

Seung Hyun Kim, Si-Wouk Kim, Soo Jeong Choi, Yong-Chul Kim and Tae Sung Kim*



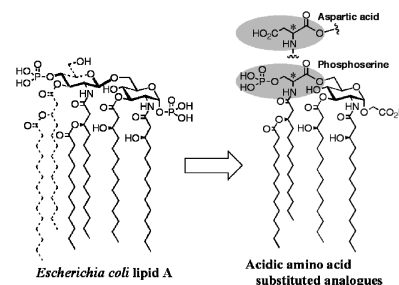
Leukemia may eventually be treated with agents that induce terminal differentiation. In this study, we investigated a possible enhancement of indirubin derivatives on differentiation of human myelocytic leukemia cells when combined with nontoxic concentrations of 1,25-dihydroxyvitamin D₃ or all-*trans* retinoic acid, two well-known differentiation inducers.

Synthesis of lipid A monosaccharide analogues containing acidic amino acid: Exploring the structural basis for the endotoxic and antagonistic activities

pp 6759–6777

Masao Akamatsu, Yukari Fujimoto, Mikayo Kataoka, Yasuo Suda, Shoichi Kusumoto and Koichi Fukase*

Lipid A monosaccharide analogues possessing acidic amino acid were synthesized. Aspartic acid-substituted analogues exhibited endotoxicity, and in contrast phosphoserine-substituted ones behaved as antagonists.

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

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Summary of instructions to authors

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*Corresponding author

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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