

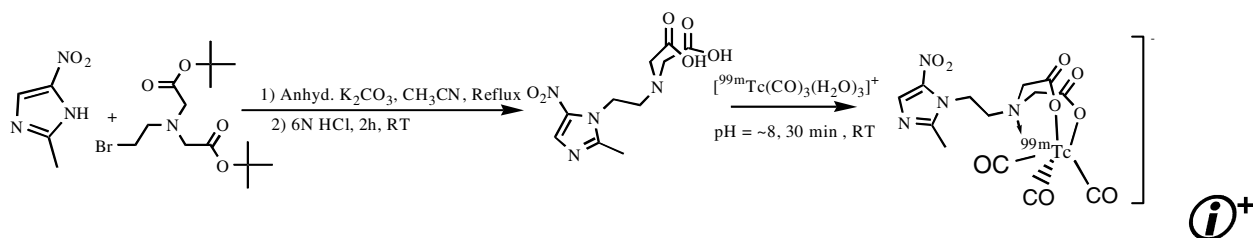
Contents

ARTICLES

Evaluation of $^{99m}\text{Tc}(\text{CO})_3$ complex of 2-methyl-5-nitroimidazole as an agent for targeting tumor hypoxia

pp 7666–7670

Madhava B. Mallia, Suresh Subramanian, Sharmila Banerjee,* H. D. Sarma and Meera Venkatesh

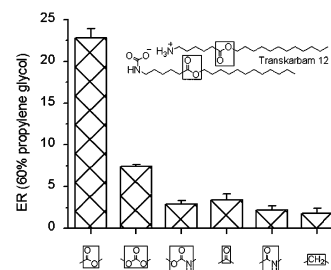


Synthesis and transdermal permeation-enhancing activity of carbonate and carbamate analogs of Transkarbam 12

pp 7671–7680

Tomáš Holas, Kateřina Vávrová,* Martin Šíma, Jana Klimentová and Alexandr Hrabálek




Ester group is essential for transdermal permeation-enhancing activity of Transkarbam 12; its replacement not only decreases the enhancing potency, but is likely to change the mechanism of action.



Influence of terminal branching on the transdermal permeation-enhancing activity in fatty alcohols and acids

pp 7681–7687

Jana Klimentová, Petr Kosák, Kateřina Vávrová, Tomáš Holas and Alexandr Hrabálek*

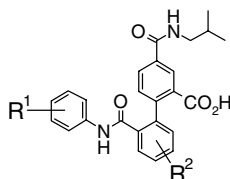
				
		x=4,6,8	x=4-8	x=6, 8
ER(x=8)	R: CH ₂ OH	12.16	11.92	18.13
	R: COOH	2.43	4.10	11.45

The influence of terminal methyl and ethyl branching on the transdermal permeation-enhancing activity (ER) was studied.

Potent and selective TF/FVIIa inhibitors containing a neutral P1 ligand

pp 7688–7705

Masanori Miura,* Norio Seki, Takanori Koike, Tsukasa Ishihara, Tatsuya Niimi, Fukushi Hirayama, Takeshi Shigenaga, Yumiko Sakai-Moritani, Tomihisa Kawasaki, Shuichi Sakamoto, Minoru Okada, Mitsuaki Ohta and Shin-ichi Tsukamoto

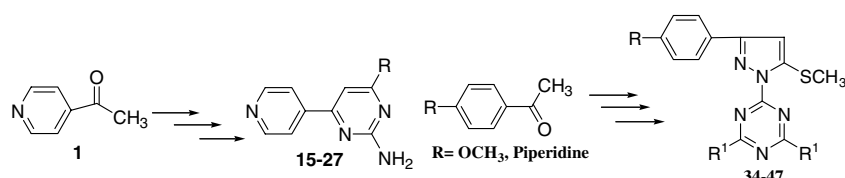


Tissue factor/factor VIIa complex (TF/FVIIa) inhibitors that contain a neutral P1 ligand were prepared and evaluated for inhibitory activity against TF/FVIIa in vitro.

Synthesis of 2,4,6-trisubstituted pyrimidine and triazine heterocycles as antileishmanial agents

pp 7706–7715

Naresh Sunduru, Anu Agarwal, Sanjay Babu Katiyar, Nishi, Neena Goyal, Suman Gupta and Prem M. S. Chauhan*

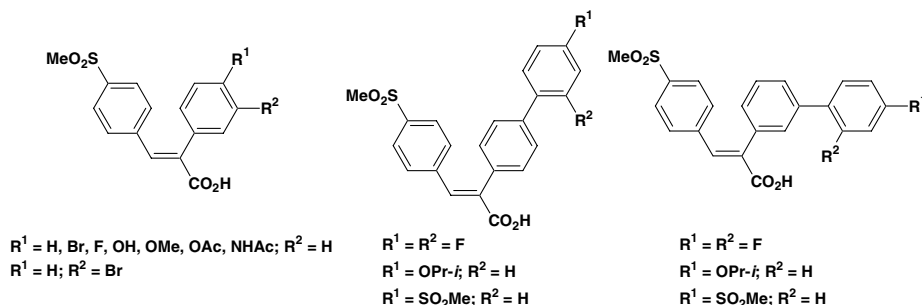


A series of 2,4,6-trisubstituted pyrimidines and triazines have been synthesized and screened for its in vitro antileishmanial activity profile in promastigote model. Nine compounds have shown >94% inhibition against promastigotes at a concentration of 10 μ g/mL.

Design, synthesis, and biological evaluation of (E)-3-(4-methanesulfonylphenyl)-2-(aryl)acrylic acids as dual inhibitors of cyclooxygenases and lipoxygenases

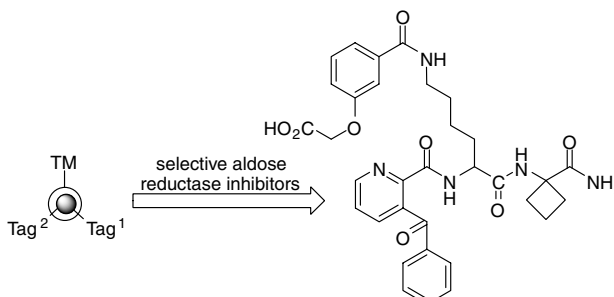
pp 7716–7727

Anne Moreau, Qiao-Hong Chen, P. N. Praveen Rao and Edward E. Knaus*

**On-bead combinatorial techniques for the identification of selective aldose reductase inhibitors**

pp 7728–7735

Lori I. Robins, Seth M. Dixon, David K. Wilson and Mark J. Kurth*

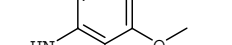


pp 7736–7744

pp 7745–7760



pp 7761–7773



5a, Hit **51**, Lead

pp 7774–7789

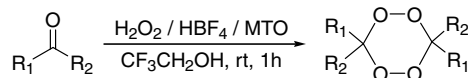
	R1	R2	R3	Ar	IC ₅₀ , μM
13	-(CH ₂) ₃ -		Me	5-Methyl-2-furyl	0.0041
15	Me	Me	H	2-Thiazolyl	0.0035
16	-(CH ₂) ₃ -		H	2-Thiazolyl	0.0040
17	Me	Me	Me	2-Thiazolyl	0.0043

Sulfonamide derivatives **13** and **15–17** were found to be highly potent and selective EP1 receptor antagonists. *In vivo* EP1 antagonist activity was also determined.

Synthesis and antimalarial activities of novel 3,3,6,6-tetraalkyl-1,2,4,5-tetraoxanes

pp 7790–7795

Katja Žmitek, Stojan Stavber, Marko Zupan, Daniele Bonnet-Delpon, Sebastien Charneau, Phillipe Grellier and Jernej Iskra*

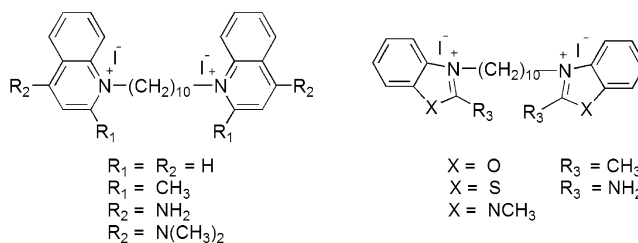


Antimalarial activities of synthesized tetraoxanes with alkyl groups of different lengths and branching were determined and their correlation with polarity as well as geometry around pharmacophoric peroxide unit was studied.

Inhibition of protein kinase C by dequalinium analogues: Structure–activity studies on head group variations

pp 7796–7803

Chandima Abeywickrama, Susan A. Rotenberg and Arthur David Baker*

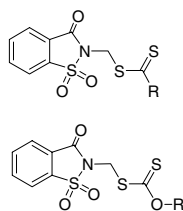


Synthesis and structure–activity studies of new dequalinium analogues and related heteroaromatic systems for protein kinase C α inhibition.

**Synthesis, antimycobacterial and antitumor activities of new (1,1-dioxido-3-oxo-1,2-benzisothiazol-2(3H)-yl)methyl *N,N*-disubstituted dithiocarbamate/*O*-alkyldithiocarbonate derivatives**

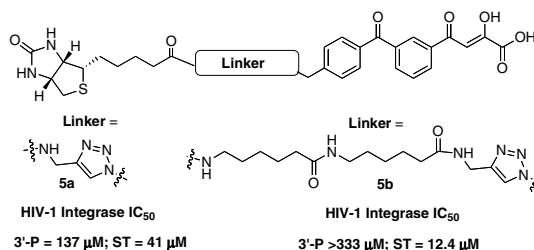
pp 7804–7815

Özlen Güzel* and Aydın Salman

**Biotinylated biphenyl ketone-containing 2,4-dioxobutanoic acids designed as HIV-1 integrase photoaffinity ligands**

pp 7816–7825

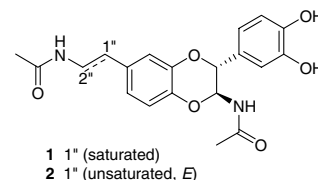
Xue Zhi Zhao, Elena A. Semenova, Chenzhong Liao, Marc Nicklaus, Yves Pommier and Terrence R. Burke, Jr.*



Antioxidant and anti-inflammatory activities of *N*-acetyldopamine dimers from *Periostracum Cicadae* pp 7826–7834

Ming-Zhe Xu, Woo Song Lee, Jong-Min Han, Hyun-Woo Oh, Doo-Sang Park, Guan-Rong Tian, Tae-Sook Jeong* and Ho-Yong Park*

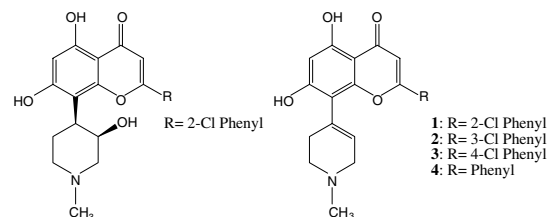
A known *N*-acetyldopamine dimer, (2*R*,3*S*)-2-(3',4'-dihydroxyphenyl)-3-acetylamino-7-(*N*-acetyl-2''-aminoethyl)-1,4-benzodioxane (**1**), and a new *N*-acetyldopamine dimer, (2*R*,3*S*)-2-(3',4'-dihydroxyphenyl)-3-acetylamino-7-(*N*-acetyl-2''-aminoethylene)-1,4-benzodioxane (**2**), were isolated from the methanolic extracts of *Periostracum Cicadae*. Compounds **1** and **2** exhibited the antioxidant activities and the anti-inflammatory activities in LPS-induced RAW264.7 cells.

**Bioactivity of glycogen phosphorylase inhibitors that bind to the purine nucleoside site**

pp 7835–7845

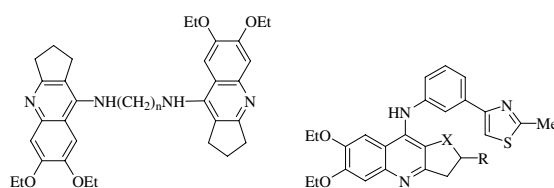
Laura J. Hampson, Catherine Arden, Loran Agius*, Minas Ganotidis, Magda N. Kosmopoulou, Costas Tiraidis, Yiannis Elemes, Constantinos Sakarellos, Demetres D. Leonidas and Nikos G. Oikonomakos*

Four olefin derivatives of flavopiridol were synthesized (**1–4**). All derivatives are potent inhibitors of glycogen phosphorylase-b. Compounds **1** and **4** inhibit glycogenolysis in hepatocytes by allosteric inhibition and by counteraction of the activation of phosphorylase-b by phosphorylase kinase.

**Design, synthesis, and biological evaluation of substituted 2,3-dihydro-1*H*-cyclopenta[*b*]quinolin-9-ylamine related compounds as fructose-1,6-bisphosphatase inhibitors**

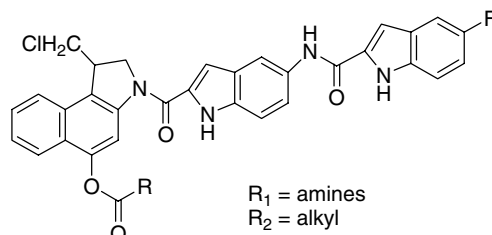
pp 7846–7853

Michela Rosini, Francesca Mancini, Andrea Tarozi, Francesco Colizzi, Vincenza Andrisano, Maria L. Bolognesi, Patrizia Hrelia and Carlo Melchiorre*

**Synthesis and antitumor activity of CBI-bearing ester and carbamate prodrugs of CC-1065 analogue**

pp 7854–7861

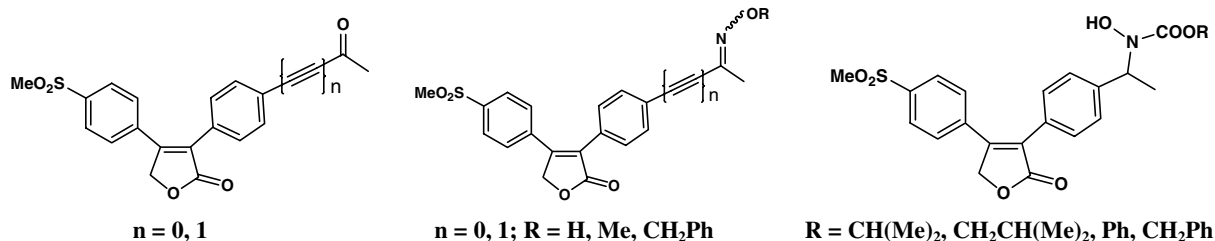
Yuqiang Wang*, Lianfa Li, Zhiming Tian, Wei Jiang and James W. Larrick



Synthesis and biological evaluation of a novel class of rofecoxib analogues as dual inhibitors of cyclooxygenases (COXs) and lipoxygenases (LOXs)

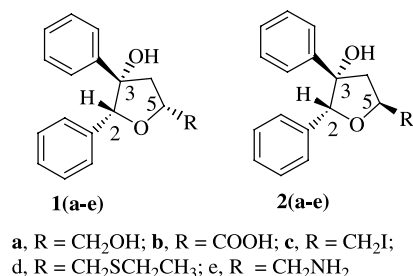
pp 7898–7909

Qiao-Hong Chen, P. N. Praveen Rao and Edward E. Knaus*

**5-Substituted-2,3-diphenyltetrahydrofurans: A new class of moderately selective COX-2 inhibitors**

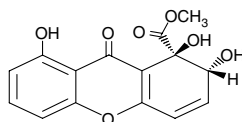
pp 7910–7916

Palwinder Singh,* Anu Mittal, Satwinderjit Kaur and Subodh Kumar*

Compounds **1b** and **2d** show appreciable inhibition and selectivity for COX-2.**A new dihydroxanthenone from a plant-associated strain of the fungus *Chaetomium globosum* demonstrates anticancer activity**

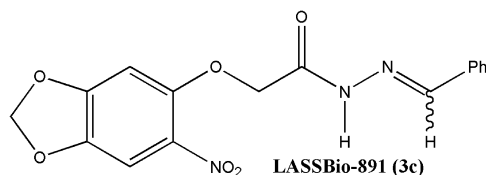
pp 7917–7923

E. M. Kithsiri Wijeratne, Thomas J. Turbyville, Anne Fritz, Luke Whitesell and A. A. Leslie Gunatilaka*

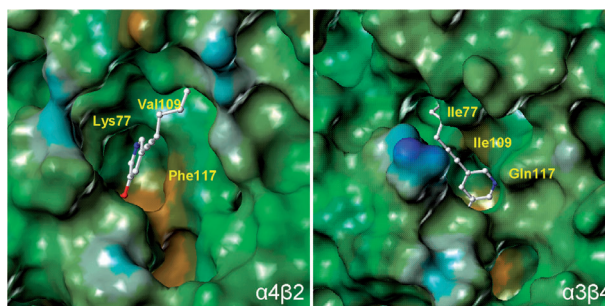
Bioassay-guided fractionation of a cytotoxic EtOAc extract of the plant-associated fungal strain, *Chaetomium globosum*, afforded a new cytotoxic and cell cycle inhibitory xanthenone, globosuxanthone A, and several other structurally related inactive metabolites.**Design and synthesis of 3,4-methylenedioxy-6-nitrophenoxyacetylhydrazone derivatives obtained from natural safrole: New lead-agents with analgesic and antipyretic properties**

pp 7924–7935

Heleno J. C. Bezerra-Netto, Daniel I. Lacerda, Ana Luisa P. Miranda, Hélio M. Alves, Eliezer J. Barreiro and Carlos A. M. Fraga*

The discovery of the new powerful analgesic and long-lasting antipyretic *N*-acylhydrazone prototype LASSBio-891 is reported.

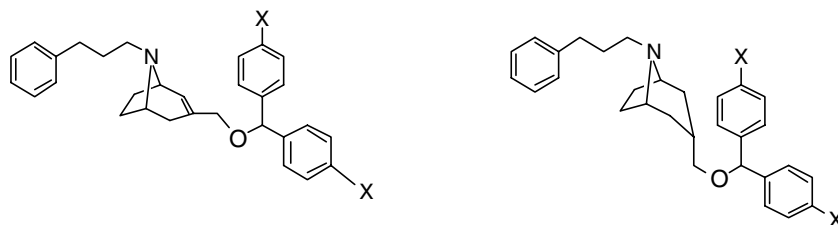
Computational evidence for the ligand selectivity to the $\alpha 4\beta 2$ and $\alpha 3\beta 4$ nicotinic acetylcholine receptors pp 7936–7942
Hongbin Yuan and Pavel A. Petukhov*



Synthesis of dopamine transporter selective 3-diarylmethoxymethyl-8-arylalkyl-8-azabicyclo[3.2.1]octane derivatives

pp 7943–7952

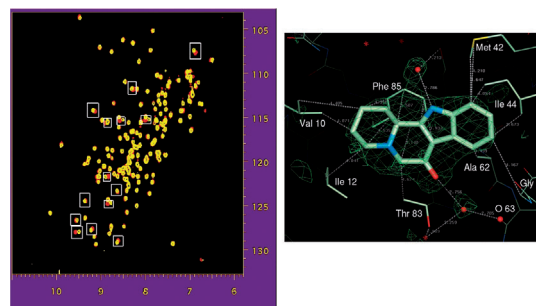
Suhong Zhang, Sari Izenwasser, Dean Wade, Liang Xu and Mark L. Trudell*



Discovery of novel inhibitors of the ZipA/FtsZ complex by NMR fragment screening coupled with structure-based design

pp 7953–7961

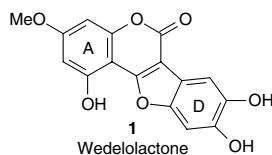
Désirée H. H. Tsao,* Alan G. Sutherland, Lee. D. Jennings,
Yuanhong Li, Thomas S. Rush, III, Juan C. Alvarez,
Weidong Ding, Elizabeth G. Dushin, Russell G. Dushin,
Steve A. Haney, Cynthia H. Kenny, A. Karl Malakian,
Ramaswamy Nilakantan and Lidia Mosyak



Structure–activity relationship of wedelolactone analogues: Structural requirements for inhibition of Na^+, K^+ -ATPase and binding to the central benzodiazepine receptor

pp 7962–7966

Elisa S. C. Pôças, Daniele V. S. Lopes, Alcides J. M. da Silva, Paulo H. C. Pimenta,
Fernanda B. Leitão, Chaquip D. Netto, Camilla D. Buarque, Flávia V. Brito,
Paulo R. R. Costa* and François Noël*



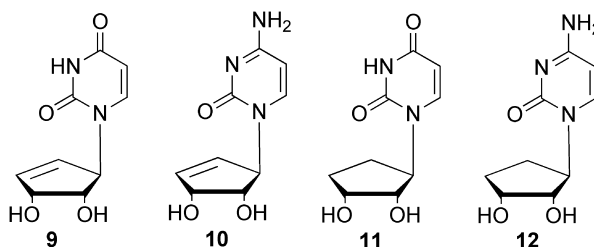
Wedelolactone and nine coumestan analogues were synthesized and a structure–activity relationship performed for their effect as inhibitors of kidney Na^+, K^+ -ATPase and ligands for the central benzodiazepine receptor.



Carbocyclic pyrimidine nucleosides as inhibitors of *S*-adenosylhomocysteine hydrolase

pp 7967–7971

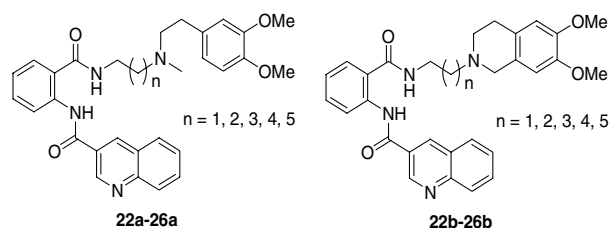
Sylvester L. Mosley, Brian A. Bakke, Joshua M. Sadler, Naresh K. Sunkara, Kathleen M. Dorgan, Zhaohui Sunny Zhou and Katherine L. Seley-Radtke*

**In vitro activity of novel dual action MDR anthranilamide modulators with inhibitory activity at CYP-450**

pp 7972–7987

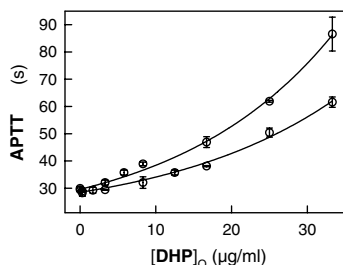
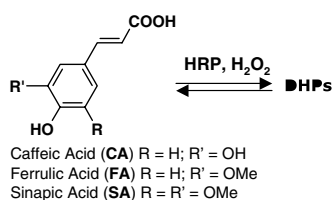
Philippe Labrie,* Shawn P. Maddaford, Jacques Lacroix, Concettina Catalano, David K. H. Lee, Suman Rakhit and René C. Gaudreault

Synthesis and in vitro cytotoxicity assays of new anthranilamide MDR modulators were performed to assess their potency to inhibit P-glycoprotein and CYP450.

**Novel chemo-enzymatic oligomers of cinnamic acids as direct and indirect inhibitors of coagulation proteinases**

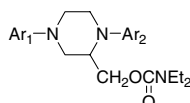
pp 7988–7998

Bernhard H. Monien, Brian L. Henry, Arjun Raghuraman, Michael Hindle and Umesh R. Desai*

**Structure–activity relationships in platelet-activating factor. Part 14: Synthesis and biological evaluation of piperazine derivatives with dual anti-PAF and anti-HIV-1 activity**

pp 7999–8013

Wafa Sallem, Nawal Serradji,* Nathalie Dereuddre-Bosquet, Georges Dive, Pascal Clayette and Françoise Heymans



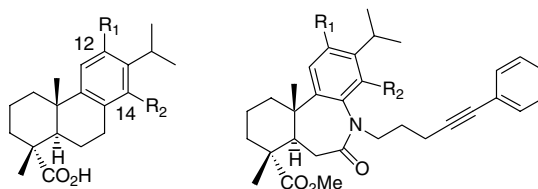
Ar₁ and/or Ar₂ = heterocyclic ring (indole, benzothiophene, quinoline, etc.); 3,4,5-(MeO)₃C₆H₂CO;
 3,4,5-(MeO)₃C₆H₂CH₂...



Design, synthesis, and BK channel-opening activity of hexahydrodibenzazepinone derivatives

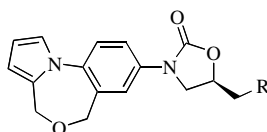
pp 8014–8031

Toshihiko Tashima, Yoshimi Toriumi, Yumi Mochizuki, Taro Nonomura, Satoru Nagaoka, Katsuo Furukawa, Hiromichi Tsuru, Satomi Adachi-Akahane and Tomohiko Ohwada*

**Substituent activity relationship studies on new azolo benzoxazepinyl oxazolidinones**

pp 8032–8042

Jagattaran Das, M. Sitaram Kumar, D. Subrahmanyam, T. V. R. S. Sastry, C. Prasad Narasimhulu, C. V. Laxman Rao, M. Kannan, M. Roshaiiah, Riti Awasthi, Santosh N. Patil, H. M. Sarnaik, N. V. S. Rao Mamidi, N. Selvakumar* and Javed Iqbal*



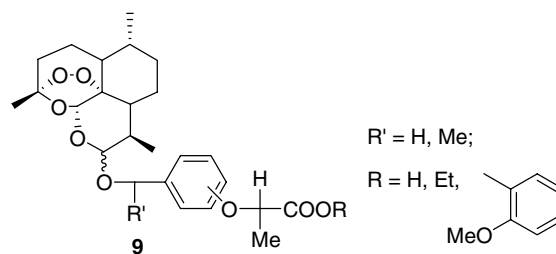
The synthesis of a series of tricyclic oxazolidinones is disclosed. SAR studies on these novel compounds and evaluation of a lead compound are reported.

Synthesis and immunosuppressive activity of new artemisinin derivatives. Part 2: 2-[12(β or α)-Dihydroartemisinoxymethyl(or 1'-ethyl)]phenoxyl propionic acids and esters

pp 8043–8049

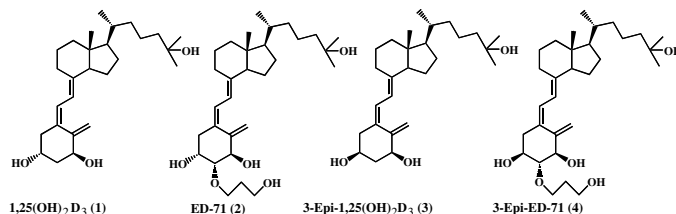
Zhong-Shun Yang, Jun-Xia Wang, Yu Zhou, Jian-Ping Zuo* and Ying Li*

Novel artemisinin derivatives **9** exhibited inhibitory effects on ConA-induced T cell and LPS-induced B cell proliferation comparable to or more potent than parent artemisinin.

**Synthesis and evaluation of a 3-position diastereomer of 1 α ,25-dihydroxy-2 β -(3-hydroxypropoxy)vitamin D₃ (ED-71)**

pp 8050–8056

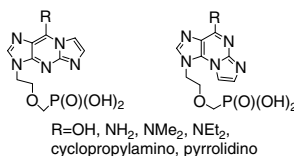
Susumi Hatakeyama, Satoshi Nagashima, Naoko Imai, Keisuke Takahashi, Jun Ishihara, Atsuko Sugita, Takeshi Nihei, Hitoshi Saito, Fumiaki Takahashi and Noboru Kubodera*



Tricyclic etheno analogs of PMEG and PMEDAP: Synthesis and biological activity

pp 8057–8065

Kateřina Hořejší, Graciela Andrei, Erik De Clercq, Robert Snoeck, Radek Pohl and Antonín Holý*

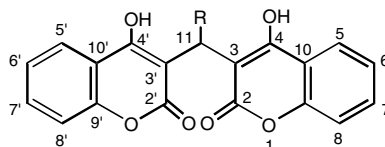


A series of novel tricyclic etheno analogs of acyclic nucleoside phosphonates PMEG and PMEDAP was synthesized and evaluated for their cytostatic and antiviral activity.

New biscoumarin derivatives-cytotoxicity and enzyme inhibitory activities

pp 8066–8072

Muhammad Iqbal Choudhary,* Naheed Fatima, Khalid M. Khan, Saima Jalil, Sajjid Iqbal and Atta-ur-Rahman



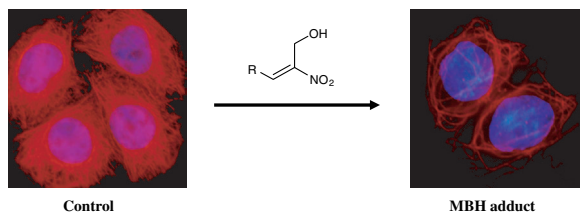
A series of biscoumarin derivatives were screened for their cytotoxicity and enzyme inhibition activity against phosphodiesterase 1 from snake venom, and human nucleotide pyrophosphatase phosphodiesterase-1. K_i and IC_{50} values of biscoumarins were found to be in the range of 50 to 1000 and 164 to >1000 μ M against the human recombinant phosphodiesterase 1 enzyme, and 8.0 to 1150 and 9.44 to >1000 μ M against the snake venom phosphodiesterase 1. Most of the active compounds were found to be non-cytotoxic and non-competitive inhibitors.

**Synthesis and evaluation of α -hydroxymethylated conjugated nitroalkenes for their anticancer activity: Inhibition of cell proliferation by targeting microtubules**

pp 8073–8085

Renu Mohan, Namrata Rastogi, Irishi N. N. Namboothiri,* Shaikh M. Mobin and Dulal Panda*

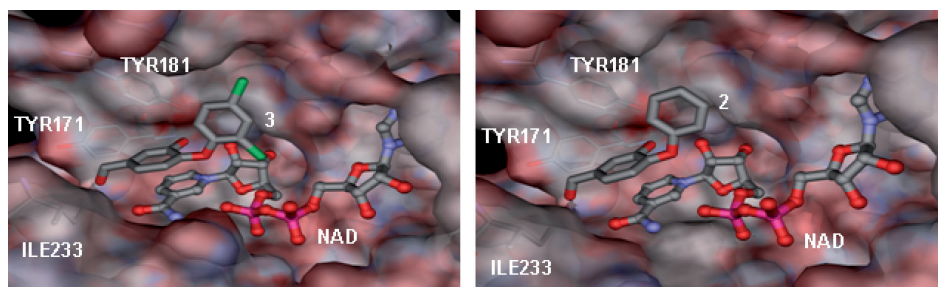
α -Hydroxymethylated conjugated nitroalkenes, synthesized by the Morita–Baylis–Hillman (MBH) reaction, inhibited HeLa cancer cell proliferation at low micromolar concentrations. The tested nitroalkenes depolymerized cellular microtubules through tubulin binding.

**Novel diphenyl ethers: Design, docking studies, synthesis and inhibition of enoyl ACP reductase of *Plasmodium falciparum* and *Escherichia coli***

pp 8086–8098

Manmohan Chhibber, Gyanendra Kumar, Prasanna Parasuraman, T. N. C. Ramya, Namita Surolia and Avadhesh Surolia*

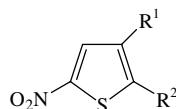
Novel diphenyl ether compounds inhibit the enoyl-acyl carrier protein reductase of *Plasmodium falciparum* and *Escherichia coli*. Some of these compounds also show potency against in vitro cultures of the two pathogens.



Structure–activity relationships in nitrothiophenes

pp 8099–8108

John O. Morley* and Thomas P. Matthews

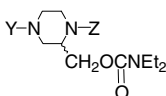


Calculated properties of nitrothiophenes versus their biological activity The calculated properties of 2-nitrothiophenes show a reasonable correlation with their experimental activity against *Escherichia coli* and *Micrococcus luteus*.

Structure–activity relationships in platelet-activating factor. Part 13: Synthesis and biological evaluation of piperazine derivatives with dual anti-PAF and anti-HIV-1 or pure antiretroviral activity

pp 8109–8125

Nawal Serradji,* Okkacha Bensaid, Marc Martin, Wafa Sallem, Nathalie Dereuddre-Bosquet, Houcine Benmehdi, Catherine Redeuilh, Aazdine Lamouri, Georges Dive, Pascal Clayette and Françoise Heymans

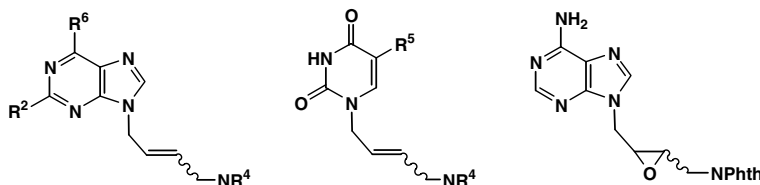


Y and/or Z = aromatic, polyaromatic or heterocyclic ring containing moities

**Synthesis, X-ray crystal structural study, antiviral and cytostatic evaluations of the novel unsaturated acyclic and epoxide nucleoside analogues**

pp 8126–8138

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R² = H, NHAc R⁴ = H, Phth
R⁶ = NH₂, O, Cl R⁵ = H, F, CF₃

**OTHER CONTENTS**

Summary of instructions to authors

p I

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Supplementary data available via ScienceDirect

COVER

α -hydroxymethylated nitroalkenes inhibit cancer cell proliferation apparently by depolymerizing microtubules. Shown are microtubules (red) and chromosomes (blue). Control cells are on the left and nitroalkene treated cells are on the right. [Mohan, R.; Rastogi, N.; Namboothiri, I. N. N.; Mobin, S. M.; Panda, D. *Bioorg. Med. Chem.* **2006**, 14, 8069.]

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