

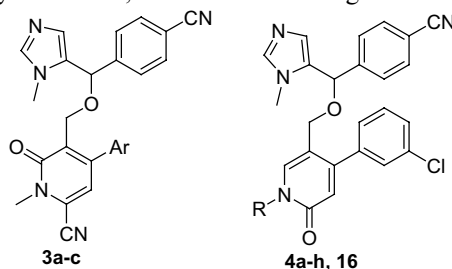
Contents

COMMUNICATIONS

Synthesis of 1H-pyridin-2-one derivatives as potent and selective farnesyltransferase inhibitors

pp 4603–4606

Le Wang,* Nan-Horng Lin, Qun Li, Rodger F. Henry, Haiying Zhang, Jerome Cohen, Wen-Zhen Gu, Kennan C. Marsh, Joy L. Bauch, Saul H. Rosenberg and Hing L. Sham



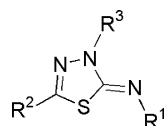
The synthesis and biological evaluation of two novel series of potent and selective FTase inhibitors are described.

Discovery of thiadiazoles as a novel structural class of potent and selective PDE7 inhibitors.

pp 4607–4613

Part 1: Design, synthesis and structure–activity relationship studies

Fabrice Vergne,* Patrick Bernardelli, Edwige Lorthiois, Nga Pham, Emmanuelle Proust, Chrystelle Oliveira, Abdel-Kader Mafroud, Frederique Royer, Roger Wrigglesworth, Jennifer K. Schellhaas, Mark R. Barvian, François Moreau, Moulay Idrissi, Anita Tertre, Bernadette Bertin, Magali Coupe, Patrick Berna and Patricia Soulard

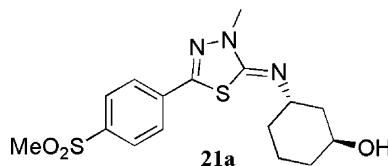


Discovery of thiadiazoles as a novel structural class of potent and selective PDE7 inhibitors.

pp 4615–4621

Part 2: Metabolism-directed optimization studies towards orally bioavailable derivatives

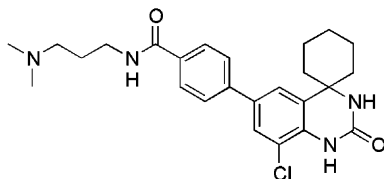
Fabrice Vergne,* Patrick Bernardelli, Edwige Lorthiois, Nga Pham, Emmanuelle Proust, Chrystelle Oliveira, Abdel-Kader Mafroud, Pierre Ducrot, Roger Wrigglesworth, Françoise Berlioz-Seux, Francis Coleon, Eric Chevalier, François Moreau, Moulay Idrissi, Anita Tertre, Arnaud Descours, Patrick Berna and Mei Li



Spiroquinazolinones as novel, potent, and selective PDE7 inhibitors. Part 1

pp 4623–4626

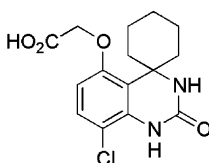
Edwige Lorthiois,* Patrick Bernardelli, Fabrice Vergne, Chrystelle Oliveira, Abdel-Kader Mafroud, Emmanuelle Proust, Lamia Heuze, François Moreau, Moulay Idrissi, Anita Tertre, Bernadette Bertin, Magali Coupe, Roger Wrigglesworth, Arnaud Descours, Patricia Soulard and Patrick Berna

**Spiroquinazolinones as novel, potent, and selective PDE7 inhibitors. Part 2:**

pp 4627–4631

Optimization of 5,8-disubstituted derivatives

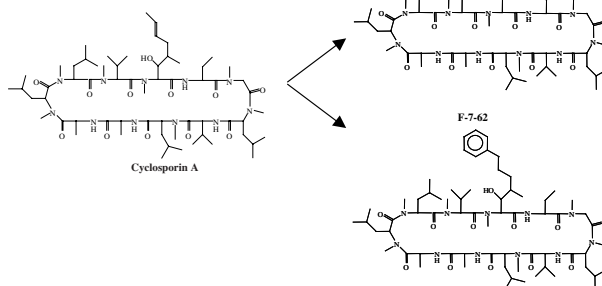
Patrick Bernardelli,* Edwige Lorthiois, Fabrice Vergne, Chrystelle Oliveira, Abdel-Kader Mafroud, Emmanuelle Proust, Nga Pham, Pierre Ducrot, François Moreau, Moulay Idrissi, Anita Tertre, Bernadette Bertin, Magali Coupe, Eric Chevalier, Arnaud Descours, Françoise Berlioz-Seux, Patrick Berna and Mei Li

**In vitro anti-parasitic activity of Cyclosporin A analogs on *Trypanosoma cruzi***

pp 4633–4637

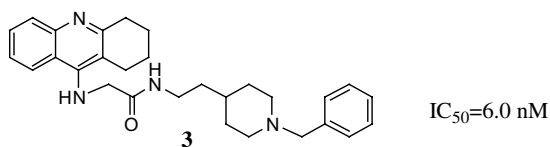
Jacqueline Búa,* Andrés M. Ruiz, Mariana Potenza and Laura E. Fichera

Cyclosporin A nonimmunosuppressive analogs were evaluated against *Trypanosoma cruzi* in vitro and on a 19 kDa *T. cruzi* cyclophilin (TcCyP19).

**Synthesis and evaluation of tacrine–E2020 hybrids as acetylcholinesterase inhibitors for the treatment of Alzheimer's disease**

pp 4639–4642

Dong Shao, Chunyan Zou, Cheng Luo, Xican Tang and Yuanchao Li*

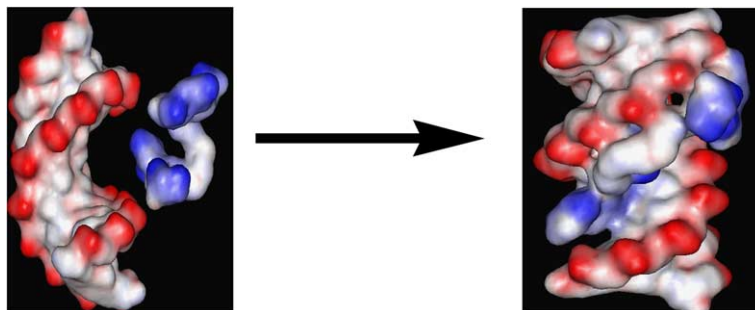


Tacrine-E2020 hybrids and some related compounds were prepared and their bioactivities on the Alzheimer's Disease were assayed. The optimum hybrid inhibitor **3** is much more potent and selective than tacrine *in vitro*.

From triplex to B-form duplex stabilization: reversal of target selectivity by aminoglycoside dimers

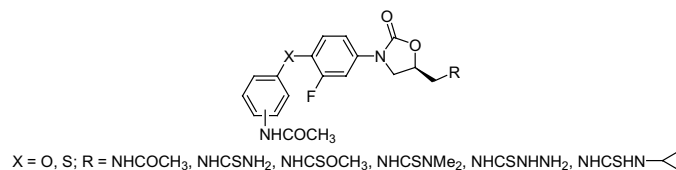
pp 4643–4646

Dev P. Arya,* R. Lane Coffee, Jr. and Liang Xue

**Synthesis and antibacterial activity of some aryloxy/thioaryloxy oxazolidinone derivatives**

pp 4647–4650

Vishal Arora, Manikrao M. Salunkhe, Neelima Sinha, Rakesh K. Sinha and Sanjay Jain*

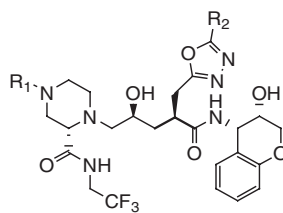


A series of aryloxy/thioaryloxy oxazolidinones has been synthesized and their antibacterial activity in vitro were evaluated and compared with linezolid.

P1' oxadiazole protease inhibitors with excellent activity against native and protease inhibitor-resistant HIV-1

pp 4651–4654

Ronald M. Kim,* Elizabeth A. Rouse, Kevin T. Chapman, William A. Schleif, David B. Olsen, Mark Stahlhut, Carrie A. Rutkowski, Emilio A. Emini and James R. Tata

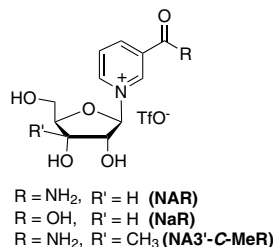


HIV-1 protease inhibitors bearing 1,3,4-oxadiazoles at the P1' position are highly active against native and PI-resistant HIV-1.

Stereoselective synthesis of nicotinamide β -riboside and nucleoside analogs

pp 4655–4658

Palmarisa Franchetti,* Michela Pasqualini, Riccardo Petrelli, Massimo Ricciutelli, Patrizia Vita and Loredana Cappellacci

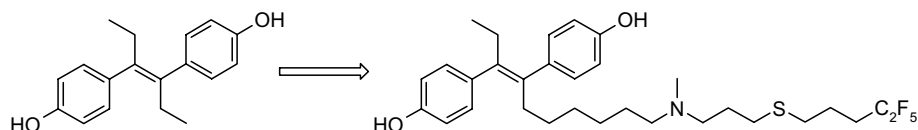


A stereoselective synthesis of β -anomers of nicotinamide riboside (NAR), its deamidated analog (NaR), and of a nicotinamide C-methylated riboside derivative (NA3'-C-MeR) was developed.

Synthesis and biological evaluation of stilbene-based pure estrogen antagonists

pp 4659–4663

Georg Walter, Renate Liebl and Erwin von Angerer*

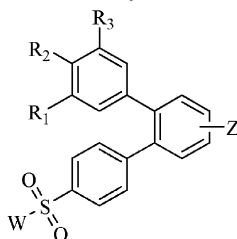


The nonsteroidal estrogen diethylstilbestrol can be converted into potent antiestrogens devoid of agonist activity by introduction of side chains with appropriate functional groups.

Exploring QSAR with E-state index: selectivity requirements for COX-2 versus COX-1 binding of terphenyl methyl sulfones and sulfonamides

pp 4665–4670

Santanu Chakraborty, Chandana Sengupta and Kunal Roy*



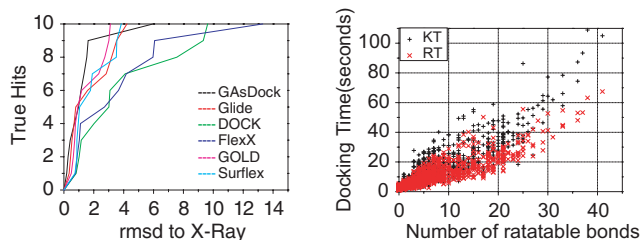
An attempt has been made to explore selectivity requirements for COX-2 versus COX-1 binding of terphenyl methyl sulfones and sulfonamides using electrotopological state (E-state) index and suitable indicator parameters.

GAsDock: a new approach for rapid flexible docking based on an improved multi-population genetic algorithm

pp 4671–4676

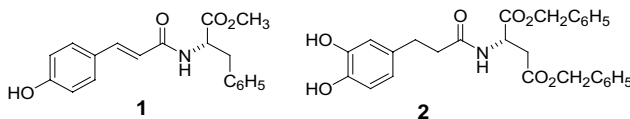
Honglin Li, Chunlian Li, Chunshan Gui, Xiaomin Luo, Kaixian Chen, Jianhua Shen,* Xicheng Wang* and Hualiang Jiang*

A new rapid accurate flexible docking program, GAsDock, was developed based on an improved multi-population genetic algorithm. Its rapid docking speed and excellent accuracy are efficient enough for virtual screening toward large-scale chemical databases.

**Synthesis of cinnamic acid derivatives and their inhibitory effects on LDL-oxidation, acyl-CoA:cholesterol acyltransferase-1 and -2 activity, and decrease of HDL-particle size**

pp 4677–4681

Sangku Lee, Jong-Min Han, Hyunjung Kim, Eungsoo Kim, Tae-Sook Jeong, Woo Song Lee and Kyung-Hyun Cho*

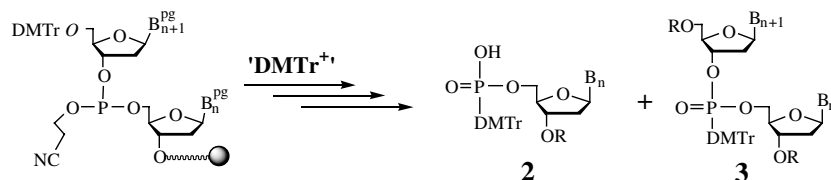


A series of cinnamic acid derivatives were prepared and their biological activities were evaluated in lipoprotein metabolism. Among the tested compounds, 4-hydroxycinnamic acid (L-phenylalanine methyl ester) amide (**1**) and 3,4-dihydroxyhydrocinnamic acid (L-aspartic acid dibenzyl ester) amide (**2**) showed potent anti-atherogenic and anti-oxidant activities.

Formation of 4,4'-dimethoxytrityl-C-phosphonate oligonucleotides

pp 4683–4690

Daniel C. Capaldi, Hans J. Gaus, Recaldo L. Carty, Max N. Moore, Brett J. Turney, Stella D. Decottignies, James V. McArdle, Anthony N. Scozzari, Vasulinga T. Ravikumar and Achim H. Krotz*

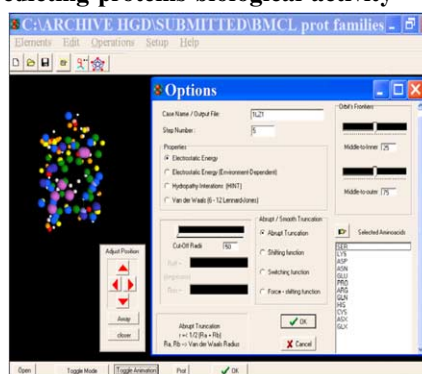


Under suboptimal sulfurization conditions DMTr-C-phosphonate monoesters **2** and DMTr-C-phosphonate diesters **3** are formed during solid-phase oligonucleotide synthesis.

Markov entropy backbone electrostatic descriptors for predicting proteins biological activity

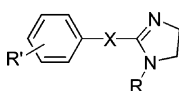
pp 4691–4695

Humberto González-Díaz,* Reinaldo Molina and Eugenio Uriarte

**2-(Anilino)imidazolines and 2-(benzyl)imidazoline derivatives as *h5*-HT_{1D} serotonin receptor ligands**

pp 4697–4699

Thomas Prisinzano, Małgorzata Dukat, Ho Law, Abdelmalik Slassi, Neil MacLean, Inés DeLannoy and Richard A. Glennon*

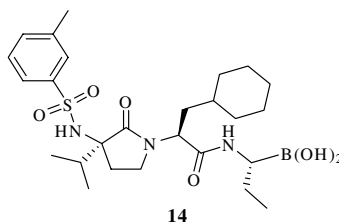


Depending on appended substituents, 2-(anilino)- and 2-(benzyl)imidazoline derivatives (X=NH or CH₂) bind at *h5*-HT_{1D} receptors with varying affinities and selectivities over *h5*-HT_{1B} receptors. Functional and pharmacokinetic data are provided for examples of 2-(benzyl)imidazolines and a ring-expanded analog: 2-(benzyl)-3,4,5,6-tetrahydropyrimidine.

Identification of a potent and rapidly reversible inhibitor of the 20S-proteasome

pp 4701–4704

Ashok V. Purandare,* Honghe Wan, Naomi Laing, Khalid Benbatoul, Wayne Vaccaro and Michael A. Poss

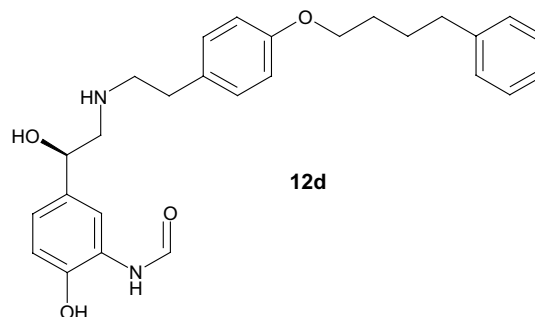


Synthesis and in vitro characterization of a novel, lactam boronic acid based, selective, and rapidly reversible inhibitor of the 20S-proteasome is presented.

Long-chain formoterol analogues: an investigation into the effect of increasing amino-substituent chain length on the β_2 -adrenoceptor activity

pp 4705–4710

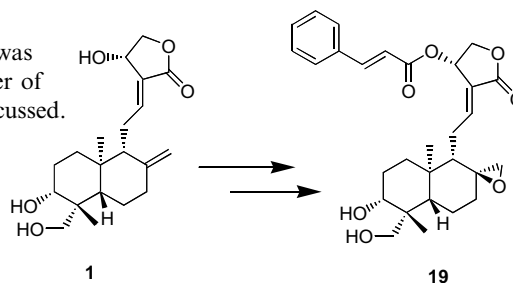
Vahid Alikhani, David Beer, David Bentley, Ian Bruce, Bernard M. Cuenoud, Robin A. Fairhurst,* Peter Gedeck, Sandra Haberthuer, Claire Hayden, Diana Janus, Lynne Jordan, Christine Lewis, Kirsty Smithies and Elke Wissler


Synthesis and structure–activity relationships of andrographolide analogues as novel cytotoxic agents

pp 4711–4717

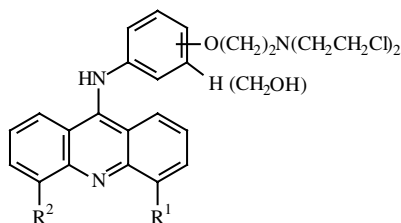
Srinivas Nanduri,* Vijay Kumar Nyavanandi, Siva Sanjeeva Rao Thunuguntla, Sridevi Kasu, Mahesh Kumar Pallerla, P. Sai Ram, Sriram Rajagopal, R. Ajaya Kumar, Rajagopalan Ramanujam, J. Moses Babu, Krishnamurthi Vyas, A. Sivalakshmi Devi, G. Om Reddy and Venkateswarlu Akella

Andrographolide **1**, the cytotoxic agent of the plant *Andrographis paniculata* was subjected to semi-synthetic studies leading to the preparation **19** and a number of related novel analogues. Synthesis and structure–activity relationships are discussed.


Potent antitumor N-mustard derivatives of 9-anilinoacridine, synthesis and antitumor evaluation

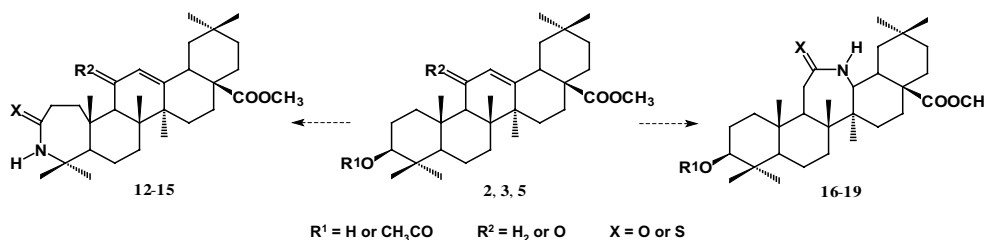
pp 4719–4722

Valeriy A. Bacherikov, Ting-Chao Chou, Hua-Jin Dong, Ching-Huang Chen, Yi-Wen Lin, Tsong-Jen Tsai and Tsann-Long Su*


Triterpenoids. Part 21: Oleanolic acid azaderivatives as percutaneous transport promoters

pp 4723–4726

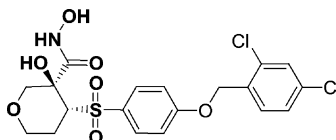
Lucjusz Zaprutko,* Danuta Partyka and Barbara Bednarczyk-Cwynar



3-Hydroxy-4-arylsulfonyltetrahydropyran-3-hydroxamic acids are novel inhibitors of MMP-13 and aggrecanase

pp 4727–4730

Mark C. Noe,* Sheri L. Snow, Lilli A. Wolf-Gouveia, Peter G. Mitchell, Lori Lopresti-Morrow, Lisa M. Reeves, Sue A. Yocum, Jennifer L. Liras and Marcie Vaughn

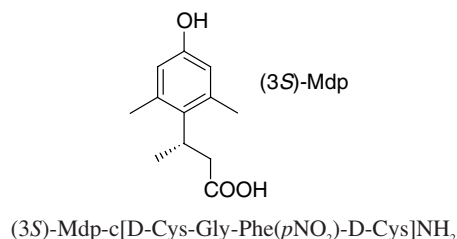


N-Hydroxy-3-hydroxy-4-arylsulfonyltetrahydropyran-3-carboxamides were designed as novel inhibitors of MMP-13 and aggrecanase based on known endocyclic hydroxamate inhibitors of matrix metalloproteinases. These compounds offer favorable physicochemical properties and low metabolic clearance. Synthesis and structure–activity relationships are reported.

A novel cyclic enkephalin analogue with potent opioid antagonist activity

pp 4731–4733

Grazyna Weltrowska, Yixin Lu, Carole Lemieux, Nga N. Chung and Peter W. Schiller*

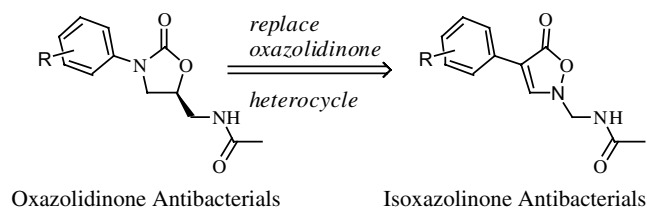


The synthesis and in vitro activity profile of a potent opioid peptide antagonist lacking an N-terminal amino group are described.

Discovery of isoxazolinone antibacterial agents. Nitrogen as a replacement for the stereogenic center found in oxazolidinone antibacterials

pp 4735–4739

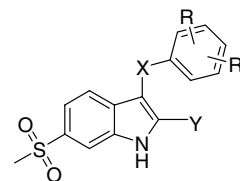
Lawrence B. Snyder,* Zhaoxing Meng, Robert Mate, Stanley V. D'Andrea, Anne Marinier, Claude A. Quesnelle, Patrice Gill, Kenneth L. DenBleyker, Joan C. Fung-Tomc, MaryBeth Frosco, Alain Martel, John F. Barrett and Joanne J. Bronson

**Rational design of 6-methylsulfonylindoles as selective cyclooxygenase-2 inhibitors**

pp 4741–4745

Jeffrey A. Campbell,* Viola Bordunov, Chris A. Broka, Michelle F. Browner, James M. Kress, Tara Mirzadegan, Chakk Ramesha, Bong F. Sanpablo, Russell Stabler, Patricia Takahara, Armando Villasenor, Keith A. M. Walker, Jin-Hai Wang, Mary Welch and Paul Weller

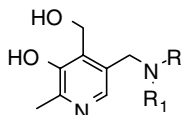
The introduction of 3-arylmethyl, 3-aryloxy and 3-arylthio moieties into a 6-methylsulfonylindole framework using rational drug design led to potent, selective COX-2 inhibitors having efficacy in a rat carrageenan air pouch model. Incorporation of a conformationally more rigid 3-aryloxy substituent onto the 6-methylsulfonylindole scaffold led to selective, but considerably less potent COX-2 inhibitors. Variation of the hydrophilicity and size of the indole 2-substituent of 3-arylthio-6-methylsulfonylindole inhibitors led to modulation of the COX-2 human whole blood (HWB) potency and selectivity.



Pyridoxine as a template for the design of antiplatelet agents

pp 4747–4750

Wenlian Zhang, John Yao, Vinh Pham, Tara Whitney, Doug Froese, Albert D. Friesen, Linda Stang, Chen Xu, Ashfaq Shuaib, James M. Diakur and Wasim Haque*

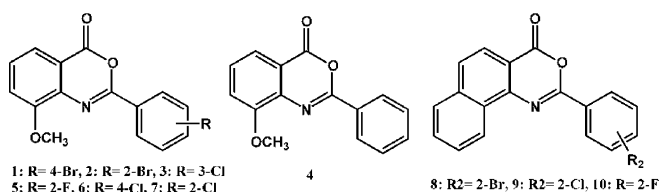


We describe the synthesis and biological activity of novel pyridoxine derivatives as potential antiplatelet agents.

2-Substituted benzoxazinone analogues as anti-human coronavirus (anti-HCoV) and ICAM-1 expression inhibition agents

pp 4751–4754

Pei-Wen Hsieh, Fang-Rong Chang, Cheng-Hsien Chang, Pei-Wen Cheng, Lien-Chai Chiang, Fu-Long Zeng, Kuei-Hsiang Lin and Yang-Chang Wu*

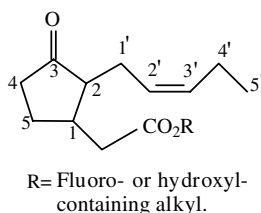


A series of 2-substituted benzoxazinones were synthesized and showed significant effect to anti-human coronavirus and ICAM-1 expression inhibition.

Novel fluoro- and hydroxyl-containing jasmonate derivatives as highly efficient elicitors in suspension cultures of *Taxus chinensis*

pp 4755–4758

Zhenjiang Zhao, Yufang Xu, Zhigang Qian, Wenhong Tian, Xuhong Qian* and Jian-Jiang Zhong*

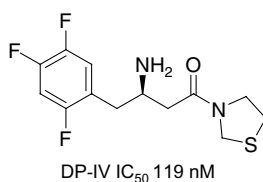


Some of jasmonate derivatives with fluoro- or hydroxyl groups on their ester parts are found to be novel and effective elicitors, which enhanced the production of taxuyunnanin C (Tc) up to 60% more than that by methyl jasmonate in *Taxus chinensis* cell cultures.

Discovery of potent and selective β -homophenylalanine based dipeptidyl peptidase IV inhibitors

pp 4759–4762

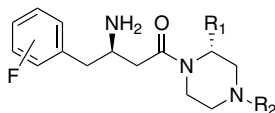
Jinyou Xu,* Hyun O. Ok, Edward J. Gonzalez, Lawrence F. Colwell, Jr., Bahanu Habulihaz, Huaibing He, Barbara Leiting, Kathryn A. Lyons, Frank Marsilio, Reshma A. Patel, Joseph K. Wu, Nancy A. Thornberry, Ann E. Weber and Emma R. Parmee



Substituted piperazines as novel dipeptidyl peptidase IV inhibitors

pp 4763–4766

Linda L. Brockunier,* Jiafang He, Lawrence F. Colwell, Jr., Bahanu Habulihaz, Huaibing He, Barbara Leiting, Kathryn A. Lyons, Frank Marsilio, Reshma A. Patel, Yohannes Teffera, Joseph K. Wu, Nancy A. Thornberry, Ann E. Weber and Emma R. Parmee

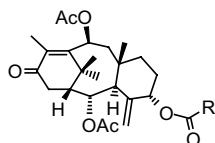


The synthesis and SAR of a series of piperazines containing a fluorophenyl β -amino amide moiety is reported.

Synthesis and biological evaluation of taxinine analogues as orally active multidrug resistance reversal agents in cancer

pp 4767–4770

Xin Zhao, Jun Gu, Dali Yin and Xiaoguang Chen*



8: R = PhCH₂

9: R = PhCH₂CH₂

10: R = 2,5- dimethoxyl-PhCH₂

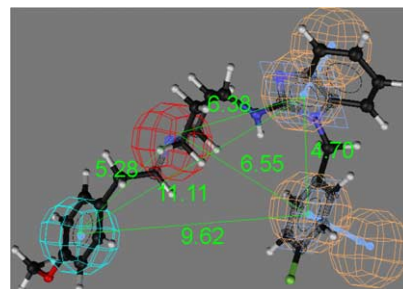
Three novel taxinine analogues were prepared and tested for their activity as multidrug resistance (MDR) reversal agents in comparison with verapamil. In vitro testing demonstrated that compounds **8–10** possess MDR-reversal activity in the KB/V cell line. In accumulation assay, the intracellular rhodamine123 concentration increased significantly after treatment with compound **9**, higher than that of verapamil in KB/V cell line. In vivo studies with VCR-resistant KB/V tumor xenografts showed that **9** in combination with VCR significantly inhibited tumor growth. Treatment with VCR or **9** alone did not result in growth inhibition.

The pharmacophore hypotheses of I_{Kr} potassium channel blockers: novel class III antiarrhythmic agents

pp 4771–4777

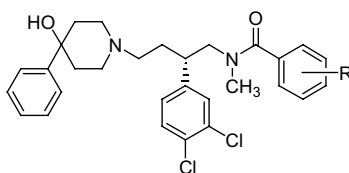
Lü-Pei Du, Keng-Chang Tsai, Min-Yong Li, Qi-Dong You* and Lin Xia

This paper reports a pharmacophore hypothesis for I_{Kr} potassium channel blockers using HypoGen module in Catalyst software. The pharmacophore can be used to in predicting biological activity of compounds by virtual screening.

**Design and synthesis of substituted N-methylbenzamide analogues derived from SR 48,968 as neurokinin-2 receptor antagonists**

pp 4779–4782

Shih-Chung Huang, Bradley J. Udem and Vijaya L. Korlipara*



R = H

R = *p*-F

R = *o*-, *m*-, *p*-NO₂

R = *o*-, *m*-, *p*-NH₂

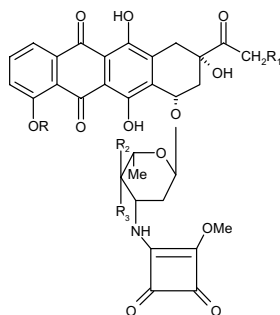
R = *o*-, *m*-, *p*-NCS

R = *o*-, *m*-, *p*-NHCOCH₃

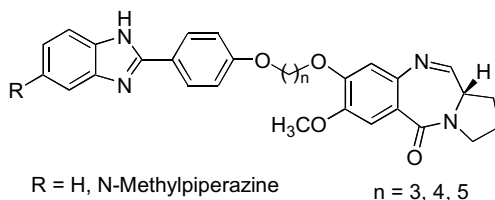
R = *o*-, *m*-, *p*-NHCOCH₂Br

Formation of squaric acid amides of anthracycline antibiotics. Synthesis and cytotoxic properties**pp 4783–4789**

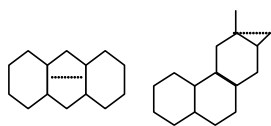
Anna Tevyashova, Ferenc Sztaricskai,* Gyula Batta, Pál Herczegh and András Jeney

**Synthesis of C8-linked pyrrolo[2,1-c][1,4]benzodiazepine–benzimidazole conjugates with remarkable DNA-binding affinity****pp 4791–4794**

Ahmed Kamal,* P. Ramulu, O. Srinivas, G. Ramesh and P. Praveen Kumar

**Topological estimation of electronic absorption bands of arene absorption spectra as a tool for modeling their toxicity and environmental pollution****pp 4795–4801**

Padmakar V. Khadikar,* Shalini Singh, Mona Jaiswal and Dheeraj Mandloi




A novel application of distance-based topological indices have been used for modeling electronic absorption bands of arene absorption spectra as a tool for modeling their toxicity and environment pollution. The statistical analysis of the data have shown that PI index gives better results for modeling $\ln \lambda_{\beta}$; while Sz index proved better for modeling $\ln \lambda_p$. The results are critically discussed on the basis of regression parameters and quality of correlation. Such a study will be useful as a tool for modeling toxicity of arene system as well as their environmental pollution.

OTHER CONTENTS

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Instructions to contributors

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pp III–VI

*Corresponding author

 Supplementary data available via ScienceDirect

COVER

Cover figure provided by **Indraneel Ghosh**, Department of Chemistry, University of Arizona. The cover depicts the **Dual Surface Selection** methodology developed by the author: the blue helix of htBI (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htBI (center) allows for functional selection against thrombin (right) [Rajagopal, S.; Meza-Romero, R.; Ghosh, I. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1389].



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