

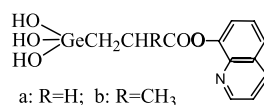
Contents

COMMUNICATIONS

DNA binding specificity and cytotoxicity of novel antitumor agent Ge132 derivatives

pp 2962–2965

Guoqiang Shanguan, Feifei Xing, Xiaogang Qu,* Jianhua Mao, Dan Zhao, Xuejian Zhao and Jinsong Ren



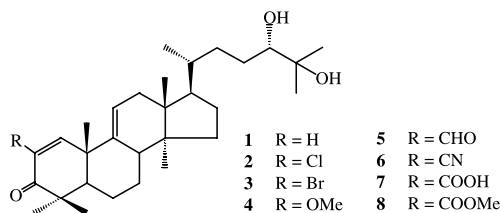
Two newly synthesized Ge132 derivatives can greatly enhance their DNA binding. Unexpected methyl substitution effect on DNA sequence selectivity and cytotoxicity was observed.



Synthetic lanostane-type triterpenoids as inhibitors of DNA topoisomerase II

pp 2966–2969

Shun-ichi Wada* and Reiko Tanaka

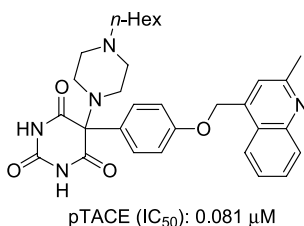


Lanostane-type triterpenoids with various functional groups (–Cl, –Br, –OMe, –CHO, –CN, –COOH, and –COOMe) at C-2 were synthesized from 3-oxolanost-9(11)-en-24S,25-diol isolated from *Pinus luchuensis* and their inhibitory effects on Topo II activity and cytotoxic activities against A549 cells were examined.

Non-hydroxamate 5-phenylpyrimidine-2,4,6-trione derivatives as selective inhibitors of tumor necrosis factor- α converting enzyme

pp 2970–2973

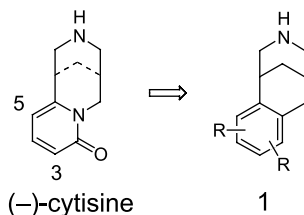
James J.-W. Duan,* Zhonghui Lu, Zelda R. Wasserman, Rui-Qin Liu, Maryanne B. Covington and Carl P. Decicco



In pursuit of $\alpha 4\beta 2$ nicotinic receptor partial agonists for smoking cessation: Carbon analogs of (–)-cytisine

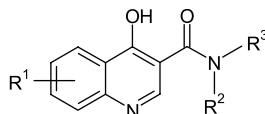
pp 2974–2979

Jotham W. Coe,* Michael G. Vetelino, Crystal G. Bashore, Michael C. Wirtz, Paige R. Brooks, Eric P. Arnold, Lorraine A. Lebel, Carol B. Fox, Steven B. Sands, Thomas I. Davis, David W. Schulz, Hans Rollema, F. David Tingley, III and Brian T. O'Neill


Design, synthesis, and biological evaluation of novel 4-hydro-quinoline-3-carboxamide derivatives as an immunomodulator

pp 2980–2985

Jun-Feng He,* Liu-Hong Yun, Ri-Fang Yang, Zhi-Yong Xiao, Jun-Ping Cheng, Wen-Xia Zhou and Yong-Xiang Zhang

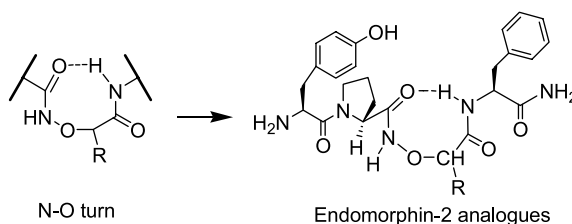


A series of novel quinoline-3-carboxamide derivatives were synthesized and evaluated for their immunomodulatory activity.

Structure–activity relationships of novel endomorphin-2 analogues with N–O turns induced by α -aminoxy acids

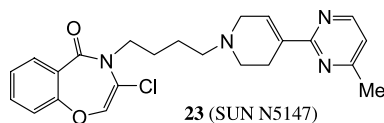
pp 2986–2989

Jie Wei, Xuan Shao, Maozhen Gong, Beibei Zhu, Yuxin Cui, Yanfeng Gao and Rui Wang*


New piperidinyl- and 1,2,3,6-tetrahydropyridinyl-pyrimidine derivatives as selective 5-HT_{1A} receptor agonists with highly potent anti-ischemic effects

pp 2990–2993

Katsuhide Kamei,* Noriko Maeda, Ryoko Katsuragi-Ogino, Makoto Koyama, Mika Nakajima, Toshio Tatsuoka, Tomochika Ohno and Teruyoshi Inoue

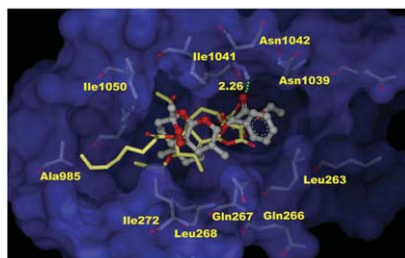


4-Methyl-2-(1,2,3,6-tetrahydropyridin-4-yl)pyrimidine derivative **23** (SUN N5147) exhibited sub-nanomolar affinity for 5-HT_{1A} receptor with 1000-fold selectivity over both dopamine D₂ and α_1 -adrenergic receptors and remarkable neuroprotective activity in a transient middle cerebral artery occlusion model.

Three-dimensional structure of *Plasmodium falciparum* Ca²⁺-ATPase(PfATP6) and docking of artemisinin derivatives to PfATP6

pp 2994–2997

Mankil Jung,* Hanjo Kim, Ki Youp Nam and Kyoung Tai No

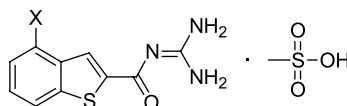


The structure of PfATP6 and docking of artemisinins to PfATP6 are reported.

4-Substituted (benzo[*b*]thiophene-2-carbonyl)guanidines as novel Na⁺/H⁺ exchanger isoform-1 (NHE-1) inhibitors

pp 2998–3001

Sunkyung Lee, Hyunsuk Lee, Kyu Yang Yi,* Byung Ho Lee, Sung-eun Yoo, Kyunghee Lee and Nam Sook Cho

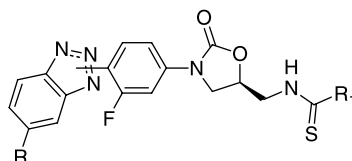


Synthesis and biological evaluation of 4-substituted (benzo[*b*]thiophene-2-carbonyl)guanidines as NHE-1 inhibitors are reported.

Synthesis and antibacterial activity of novel (un)substituted benzotriazolyl oxazolidinone derivatives

pp 3002–3005

Prasad P. Dixit, Prathap S. Nair, Vijaykumar J. Patil, Sanjay Jain, Sudershan K. Arora and Neelima Sinha*



R = H; R₁ = NH₂, NHCH₂CH₂OH, NHCH₂CH₂CH₂OH, NHCH₂CH₂NEt₂, OMe, OCH₂CF₃, OCH₂CF₂CHF₂, OCH₂CH₂OH, OCH₂CH₂NMe₂
 R = CO₂Me; R₁ = NH₂, OMe

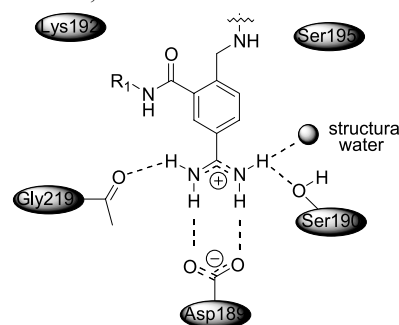
Oxazolidinone derivatives containing (un)substituted-benzotriazole ring were synthesized and exhibited potent in vitro antibacterial activity against many antibiotic-resistant microbial strains. Several analogues from this series were comparable or more potent than linezolid in vitro.

Structure-based design and synthesis of pyrazinones containing novel P₁ ‘side pocket’ moieties as inhibitors of TF/VIIa

pp 3006–3011

Barbara A. Schweitzer,* William L. Neumann, Hayat K. Rahman, Carrie L. Kusturin, Kirby R. Sample, Gennadiy I. Poda, Ravi G. Kurumbail, Anna M. Stevens, Roderick A. Stegeman, William C. Stallings and Michael S. South

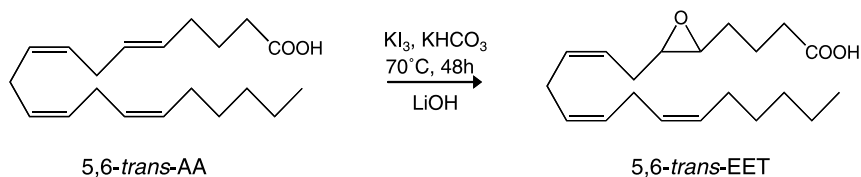
We used structure-based design to develop novel TF/VIIa inhibitors containing a P₁ side pocket moiety that engages Lys192 and Gly216 as demonstrated in an enzyme/inhibitor X-ray crystal structure.



Stereospecific synthesis and mass spectrometry of 5,6-*trans*-epoxy-8*Z*,11*Z*,14*Z*-eicosatrienoic acid

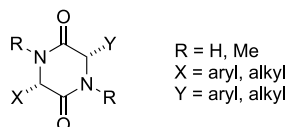
pp 3029–3033

Uzzal Roy, Russell L. Stark, Robert Joshua and Michael Balazy*

**Synthesis of a small library of diketopiperazines as potential inhibitors of calpain**

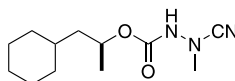
pp 3034–3038

Yibin Zeng, Qingshan Li, Robert P. Hanzlik and Jeffrey Aube*

**Acyclic cyanamide-based inhibitors of cathepsin K**

pp 3039–3043

David G. Barrett, David N. Deaton,* Anne M. Hassell, Robert B. McFadyen, Aaron B. Miller, Larry R. Miller, J. Alan Payne, Lisa M. Shewchuk, Derril H. Willard, Jr. and Lois L. Wright

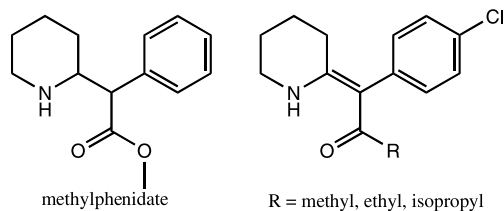


Conversion of the proline-derived cyanamide lead into an acyclic cyanamide capable of forming an additional hydrogen bond with cathepsin K resulted in a large increase in inhibitory activity. An X-ray structure of a co-crystal of a cyanamide with cathepsin K confirmed the enzyme interaction. Furthermore, a representative acyclic cyanamide inhibitor **6r** was able to attenuate bone resorption in the rat calvarial model.

Vinylogous amide analogs of methylphenidate

pp 3044–3047

Mark Froimowitz,* Yonghong Gu, Les A. Dakin, Charles J. Kelley, Damon Parrish and Jeffrey R. Deschamps

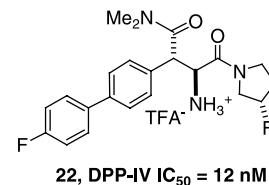


Discovery of potent and selective orally bioavailable β -substituted phenylalanine derived dipeptidyl peptidase IV inhibitors

pp 3048–3052

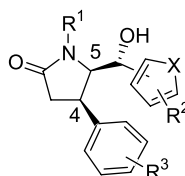
Scott D. Edmondson,* Anthony Mastracchio, Joseph L. Duffy, George J. Eiermann, Huaibing He, Ida Ita, Barbara Leiting, Joseph F. Leone, Kathryn A. Lyons, Amanda M. Makarewicz, Reshma A. Patel, Aleksandr Petrov, Joseph K. Wu, Nancy A. Thornberry and Ann E. Weber

anti-Substituted biaryl β -methylphenylalanine derived amides have been shown to be potent DPP-IV inhibitors that suffer from suboptimal selectivity and pharmacokinetics. This letter describes the substitution of the β -methyl substituent with β -polar substituents, culminating in the discovery of **22**, a β -dimethylamide substituted phenylalanine derivative with an excellent potency, selectivity, and pharmacokinetic profile.


4,5-Disubstituted *cis*-pyrrolidinones as inhibitors of type II 17 β -hydroxysteroid dehydrogenase. Part 2. SAR

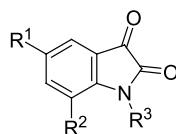
pp 3053–3057

David Gunn,* Christiana Akuche, Jeremy Baryza, Marie-Louise Blue, Catherine Brennan, Ann-Marie Campbell, Soongyu Choi, James Cook, Patricia Conrad, Brian Dixon, Jacques Dumas, Paul Ehrlich, Todd Gane, Ted Joe, Jeffrey Johnson, Jerold Jordan, Richard Kramss, Peking Liu, Joan Levy, Derek Lowe, Ian McAlexander, Reina Natero, Anikó M. Redman, William Scott, Thomas Seng, Robert Sibley, Ming Wang, Yamin Wang, Jill Wood and Zhonghua Zhang


Synthesis and evaluation of isatin derivatives as effective SARS coronavirus 3CL protease inhibitors

pp 3058–3062

Li-Rung Chen, Yu-Chin Wang, Yi Wen Lin, Shan-Yen Chou, Shyh-Fong Chen,* Lee Tai Liu,* Ying-Ta Wu, Chih-Jung Kuo, Tom Shieh-Shung Chen and Shin-Hun Juang*

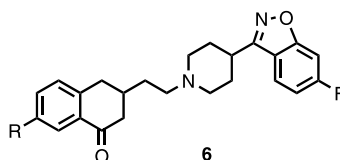


N-Substituted isatin derivatives have been prepared and their inhibition activities against SARS viral protease were evaluated.

Synthesis and binding affinity of novel 3-aminoethyl-1-tetralones, potential atypical antipsychotics

pp 3063–3066

Mario Alvarado, Alberto Coelho, Christian F. Masaguer, Enrique Raviña,* José Brea, J. Fernando Padín and María I. Loza



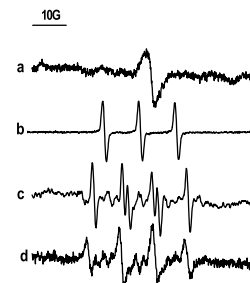
The preparation and binding affinities of new 3-aminoethyl-1-tetralones are reported. Some of these compounds (e.g., **6**) showed potential atypical antipsychotic profiles.

Synthesis and characterization of the monomer ruthenium complex of hypocrellin B

pp 3067–3070

Jiahong Zhou,^{*} Jihua Liu, Yuying Feng, Shaohua Wei, Xiaotian Gu, Xuesong Wang^{*} and Baowen Zhang^{*}

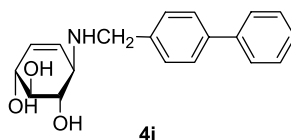
We first synthesized and characterized the monomer ruthenium complex of hypocrellin B (HB) by chelation with Ru(bpy)₂Cl₂.

**Total asymmetric synthesis of (–)-conduramine B-1 and of its enantiomer.**

pp 3071–3075

N-Benzyl derivatives of conduramine B-1 are β -glucosidase inhibitors

Robert Łysek, Catherine Schütz and Pierre Vogel^{*}

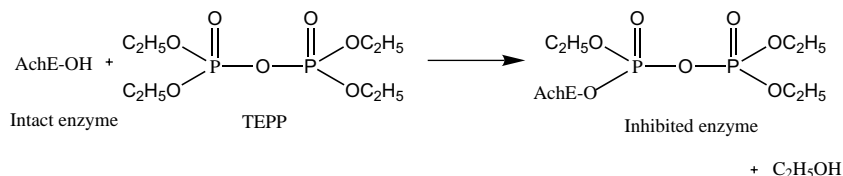


Although conduramine B-1 is not an inhibitor of β -glucosidases, *N*-benzyl derivatives inhibit these enzymes with K_i in low micromolar range. For **4i**: K_i (β -glucosidase from almond) = 8 μ M (competitive).

Quaternary salts of 4,3' and 4,4' bis-pyridinium monooximes: Synthesis and biological activity

pp 3076–3080

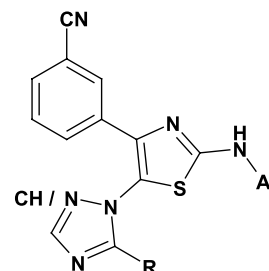
Srinivas Rao Chennamaneni, Venkateswarlu Vobalaboina^{*} and Achaiah Garlapati

**A new orally bioavailable dual adenosine A_{2B}/A₃ receptor antagonist with therapeutic potential**

pp 3081–3085

Neil J. Press,^{*} Roger J. Taylor, Joseph D. Fullerton, Pamela Tranter, Clive McCarthy, Thomas H. Keller, Lyndon Brown, Robert Cheung, Julie Christie, Sandra Habermuer, Julia D. I. Hatto, Mark Keenan, Mark K. Mercer, Nicola E. Press, Helene Sahri, Andrew R. Tuffnell, Morris Tweed and John R. Fozard

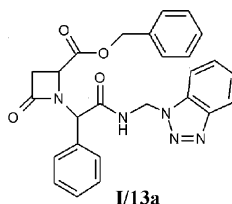
The synthesis and SAR of novel aminothiazoles as adenosine receptor antagonists is described, culminating in the synthesis of a potent and orally bioavailable dual A_{2B}/A₃ receptor antagonist.



Beta-lactam compounds as apparently uncompetitive inhibitors of HIV-1 protease

pp 3086–3090

Tamás Sperka, János Pitlik, Péter Bagossi and József Tözsér*

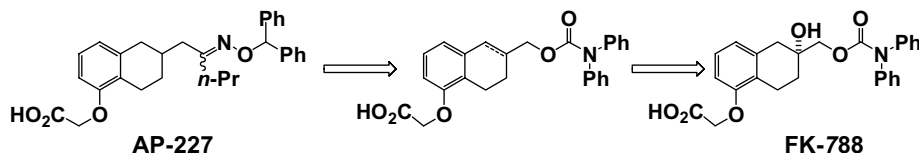


Compounds of a combinatorial monocyclic beta-lactam library were found to be apparently uncompetitive inhibitors of HIV-1 protease, providing lead compounds for a new class of HIV protease inhibitors.

Discovery of diphenylcarbamate derivatives as highly potent and selective IP receptor agonists: Orally active prostacyclin mimetics. Part 3

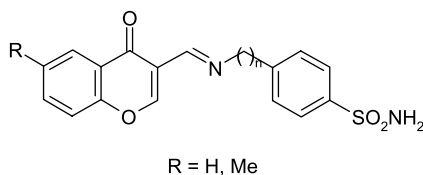
pp 3091–3095

Kouji Hattori,* Akira Tanaka, Osamu Okitsu, Seiichiro Tabuchi, Kiyoshi Taniguchi, Mie Nishio, Satoshi Koyama, Masahide Higaki, Jiro Seki and Kazuo Sakane

**Carbonic anhydrase inhibitors. Inhibition of cytosolic/tumor-associated carbonic anhydrase isozymes I, II, IX, and XII with Schiff's bases incorporating chromone and aromatic sulfonamide moieties, and their zinc complexes**

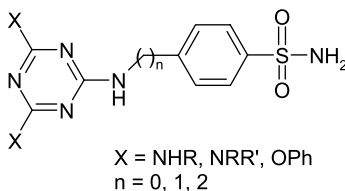
pp 3096–3101

Luca Puccetti, Giuseppe Fasolis, Daniela Vullo, Zahid H. Chohan, Andrea Scozzafava and Claudiu T. Supuran*

**Carbonic anhydrase inhibitors: Novel sulfonamides incorporating 1,3,5-triazine moieties as inhibitors of the cytosolic and tumour-associated carbonic anhydrase isozymes I, II and IX**

pp 3102–3108

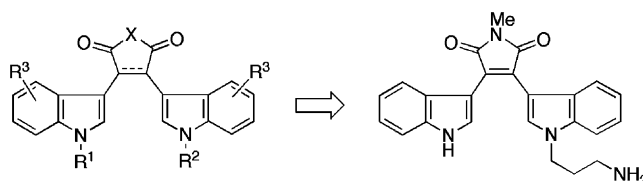
Vladimir Garaj, Luca Puccetti, Giuseppe Fasolis, Jean-Yves Winum, Jean-Louis Montero, Andrea Scozzafava, Daniela Vullo, Alessio Innocenti and Claudiu T. Supuran*



Structure–activity relationship of *N*-methyl-bisindolylmaleimide derivatives as cell death inhibitors

pp 3109–3113

Miho Katoh, Kosuke Dodo, Mikako Fujita and Mikiko Sodeoka*

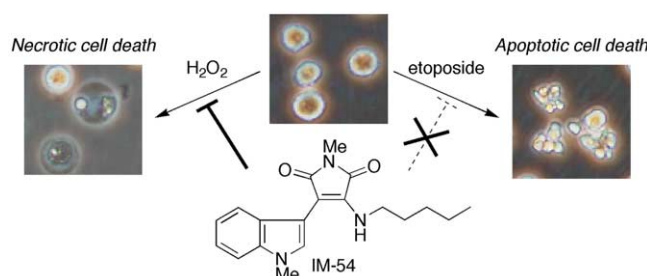


A series of *N*-methyl-bisindolylmaleimide derivatives was synthesized and evaluated as cell death inhibitors.

Inhibition of hydrogen peroxide-induced necrotic cell death with 3-amino-2-indolylmaleimide derivatives

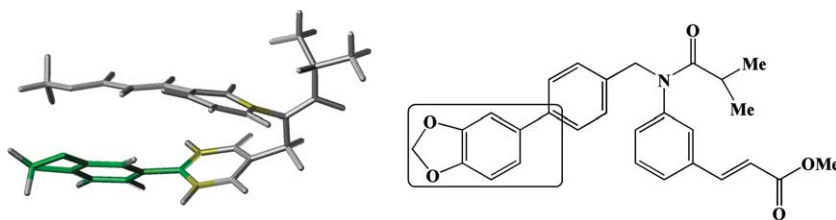
pp 3114–3118

Kosuke Dodo, Miho Katoh, Tadashi Shimizu, Masahiro Takahashi and Mikiko Sodeoka*

**Hologram quantitative structure–activity relationships for a series of farnesoid X receptor activators**

pp 3119–3125

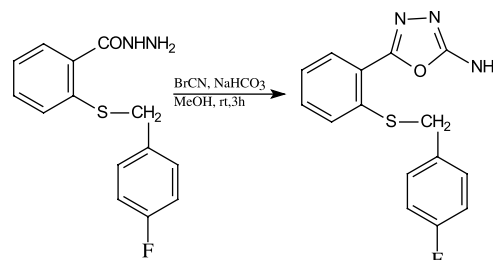
Kathia M. Honorio, Richard C. Garratt and Adriano D. Andricopulo*

**Design and synthesis of new 2-substituted-5-(2-benzylthiophenyl)-1,3,4-oxadiazoles as benzodiazepine receptor agonists**

pp 3126–3129

Afshin Zarghi,* Mehrdad Faizi, Bijan Shafaghi, Avidah Ahadian, Hamid R. Khojastehpoor, Vahideh Zanganeh, Sayyed A. Tabatabai and Abbas Shafiee

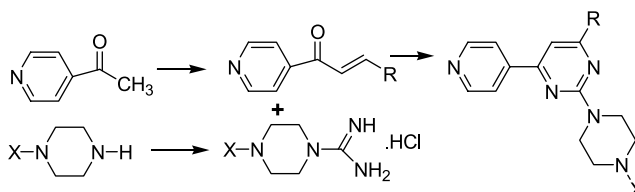
1,3,4-Oxadiazole derivatives were designed and synthesized as benzodiazepine receptor agonists. The pharmacological effect of the synthesized compounds was determined through PTZ and MES tests.



Antimalarial activity and synthesis of new trisubstituted pyrimidines

pp 3130–3132

Anu Agarwal, Kumkum Srivastava, S. K. Puri and Prem M. S. Chauhan*

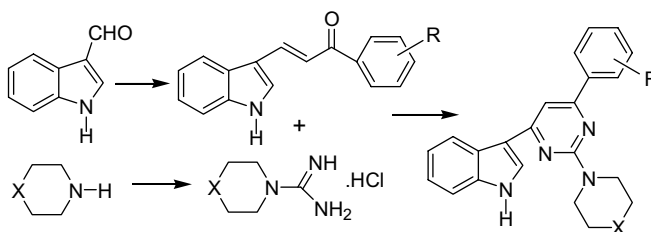


A series of 2,4,6-trisubstituted-pyrimidines was synthesized and evaluated for their in vitro antimalarial activity. Out of the 30 compounds synthesized 21 compounds showed MIC in the range of 0.5–2 $\mu\text{g/mL}$.

Synthesis of substituted indole derivatives as a new class of antimalarial agents

pp 3133–3136

Anu Agarwal, Kumkum Srivastava, S. K. Puri and Prem M. S. Chauhan*

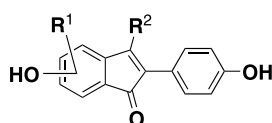


A series of substituted indole derivatives were synthesized and evaluated for their in vitro antimalarial activity against *P. falciparum*. Out of the 24 compounds synthesized six compounds have shown MIC of 1 $\mu\text{g/mL}$.

Estrogen receptor ligands: design and synthesis of new 2-arylindene-1-ones

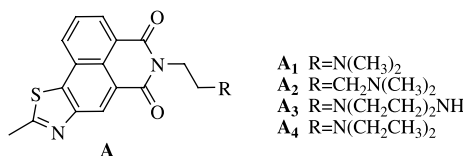
pp 3137–3142

Robert E. McDevitt,* Michael S. Malamas, Eric S. Manas, Rayomand J. Unwalla, Zhang B. Xu, Chris P. Miller and Heather A. Harris

**Synthesis, antitumor evaluation and DNA photocleaving activity of novel methylthiazonaphthalimides with aminoalkyl side chains**

pp 3143–3146

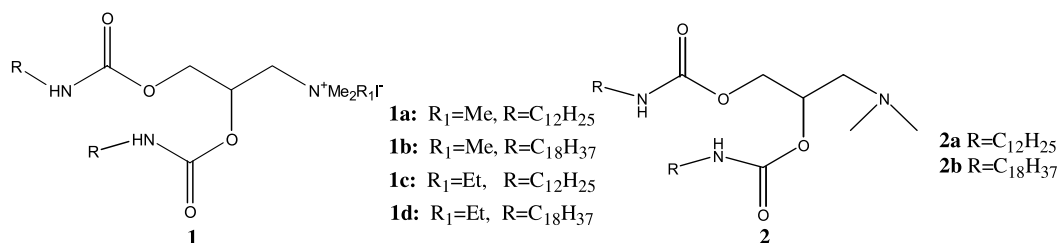
Zhigang Li, Qing Yang and Xuhong Qian*



Synthesis of carbamate-linked lipids for gene delivery

pp 3147–3150

Dongliang Liu,* Jianjun Hu, Weihong Qiao, Zongshi Li, Shubiao Zhang and Lvbo Cheng

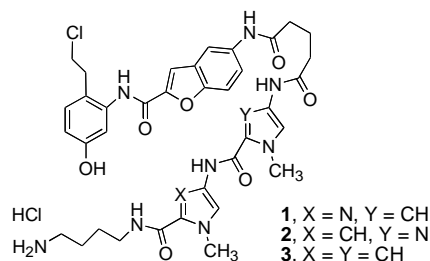


Cationic lipids **1a–d** and neutral lipids **2a,b**, with carbamate linkages between hydrocarbon chains and ammonium or tertiary amine head, which were pH sensitive, were synthesized for liposome-mediated gene delivery.

Sequence specific recognition of DNA by tailor-made hairpin conjugates of achiral *seco*-cyclopropaneindoline-2-benzofurancarboxamide and pyrrole–imidazole polyamides

pp 3151–3156

Carly A. Price, Brian M. Lingerfelt, Heather L. Handl, Konstantinos Kiakos, John A. Hartley and Moses Lee*

**Tethered phytic acid as a probe for measuring phytase activity**

pp 3157–3161

Duane F. Berry* and David A. Berry

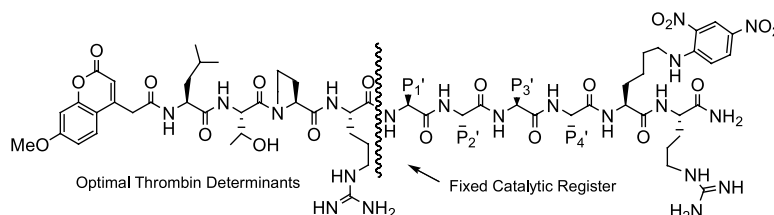
**A strategy to profile prime and non-prime proteolytic substrate specificity**

pp 3162–3166

H. Michael Petrassi, Jennifer A. Williams, Jun Li, Christine Tumanut, Jared Ek, Takashi Nakai, Brian Masick, Bradley J. Backes* and Jennifer L. Harris*

Step 1. Determine non-prime site substrate specificity with 7-amino coumarin-based PSSCLs

Step 2. Bias archived prime site substrate specificity with FRET-based PSSCLs

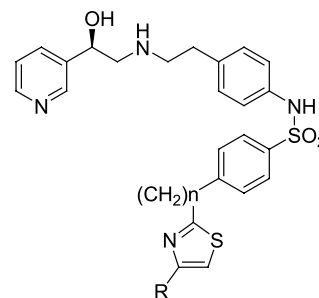


QSAR analysis of thiazole benzenesulfonamide substituted 3-pyridylethanolamines as β_3 -adrenergic receptor agonist

pp 3167–3173

P. Hanumantharao, S. V. Sambasivarao, Love K. Soni, A. K. Gupta and S. G. Kaskhedikar*

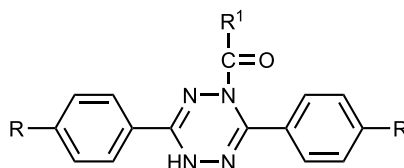
Quantitative structure–activity relationship study on a series of substituted benzene sulfonamide-3-pyridylethanolamines revealed that high electrostatic potential energy and the lipophilic nature of the molecule are favorable for β_3 -adrenergic receptor agonist activity.



Synthesis, X-ray crystallographic analysis, and antitumor activity of 1-acyl-3,6-disubstituted phenyl-1,4-dihydro-1,2,4,5-tetrazines

pp 3174–3176

Guo-Wu Rao and Wei-Xiao Hu*



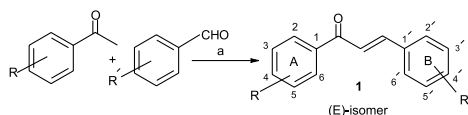
Eleven compounds were prepared by the new reactions and their structures were determined by X-ray analysis. Their antitumor activities in vitro were evaluated. The results show 1-acyl-3,6-disubstituted phenyl-1,4-dihydro-1,2,4,5-tetrazine possesses potential antitumor activities and warrants further investigation.



Synthesis and biological evaluation of chalcones and their derived pyrazoles as potential cytotoxic agents

pp 3177–3180

B. A. Bhat, K. L. Dhar,* S. C. Puri, A. K. Saxena, M. Shanmugavel and G. N. Qazi




- | | |
|---|--|
| Ia. R = R' = H | Il. R ₁ = R ₂ = R ₃ = R' = R' = OCH ₃ |
| Ib. R' = OCH ₃ | Iml. R ₁ = R ₂ = R ₃ = OCH ₃ , R' = Cl |
| Ic. R' = R' = OCH ₃ O | Iln. R ₁ = R ₂ = R ₃ = OCH ₃ , R' = F |
| Id. R' = R' = R' = OCH ₃ | Ioa. R ₁ = OCH ₃ |
| Ie. R ₁ = OH, R ₂ = R' = R' = OCH ₃ | Iop. R ₁ = R' = R' = OCH ₃ |
| If. R ₁ = OAc, R ₂ = R' = R' = OCH ₃ | Iq. R ₁ = OCH ₃ , R' = Cl |
| Ig. R ₁ = OH, R' = R' = OCH ₃ | Ir. R' = Cl |
| Ih. R ₁ = OAc, R' = R' = OCH ₃ | Iis. R ₁ = R ₂ = R ₃ = R' = OCH ₃ |
| Il. R ₁ = R' = R' = OCH ₃ | Iit. R ₁ = R ₂ = R ₃ = OCH ₃ |
| Ij. R ₁ = R ₂ = R ₃ = OCH ₃ | Iiu. R ₂ = R' = OCH ₃ |
| Ik. R ₁ = R ₂ = OCH ₃ , R' = R' = OCH ₃ O | |

OTHER CONTENTS

Contributors to this issue
Instructions to contributors

pp I–II
pp III–VI

*Corresponding author

 ⁺ Supplementary data available via ScienceDirect

COVER

2005: The proteolytic enzyme memapsin 2 (β -secretase, BACE-1) is the protease that cleaves the β -amyloid precursor protein (APP) to produce the 40–42 residue amyloid- β peptide (A β) in the human brain, a key event in the progression of Alzheimer's disease (AD). The X-ray crystal structure of memapsin 2 complexed with a peptidomimetic cyclic inhibitor is depicted. Inhibitor (green) is in the binding cleft of memapsin 2 shown as a ribbon diagram for the polypeptide backbone [Ghosh, A. K.; Devasamudram, T.; Hong, L.; DeZutter, C.; Xu, X.; Weerasena, V.; Koelsch, G.; Bilcer, G.; Tang, J. *Bioorg. Med. Chem. Lett.* **2005**, 15, 15].



Full text of this journal is available, on-line from **ScienceDirect**. Visit www.sciencedirect.com for more information.



This journal is part of **ContentsDirect**, the *free* alerting service which sends tables of contents by e-mail for Elsevier books and journals. You can register for **ContentsDirect** online at: <http://contentsdirect.elsevier.com>

Indexed/Abstracted in: Adis LMS Drug Alerts, Beilstein, Biochemistry & Biophysics Citation Index, BIOSIS previews, CAB Abstracts, CAB Health, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/Elsevier BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE



ISSN 0960-894X