

Contents

Publisher's Announcement

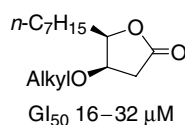
p 17

ARTICLES

Samarium(II) promoted stereoselective synthesis of antiproliferative *cis*- β -alkoxy- γ -alkyl- γ -lactones

pp 18–21

Osvaldo J. Donadel, Tomás Martín, Víctor S. Martín* and José M. Padrón*

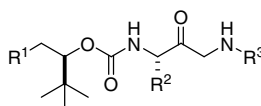


The Sm(II) promoted one-pot synthesis and the in vitro antiproliferative activity of *cis*- β -alkoxy- γ -alkyl- γ -lactones against the human solid tumor cells A2780 (ovarian cancer), SW1573 (non-small cell lung cancer) and WiDr (colon cancer) is reported.

Acyclic, orally bioavailable ketone-based cathepsin K inhibitors

pp 22–27

David G. Barrett, John G. Catalano, David N. Deaton,* Stacey T. Long, Robert B. McFadyen, Aaron B. Miller, Larry R. Miller, Vicente Samano, Francis X. Tavares, Kevin J. Wells-Knecht, Lois L. Wright and Hui-Qiang Q. Zhou

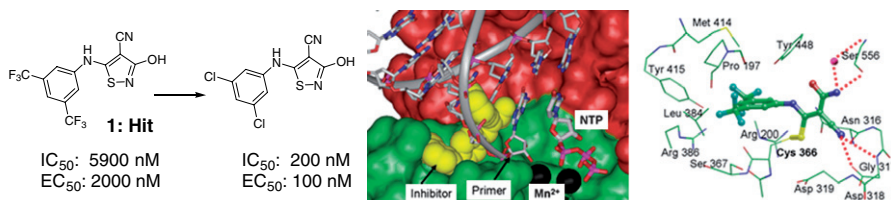


Starting from a potent ketone-based inhibitor with poor drug properties, incorporation of P²–P³ elements from a ketoamide-based inhibitor led to the identification of a hybrid series of ketone-based cathepsin K inhibitors with better oral bioavailability than the starting ketone.

Isothiazoles as active-site inhibitors of HCV NS5B polymerase

pp 28–33

Shunqi Yan,* Todd Appleby, Esmir Gunic, Jae Hoon Shim, Tania Tasu, Hongwoo Kim, Frank Rong, Huaming Chen, Robert Hamatake, Jim Z. Wu, Zhi Hong and Nanhua Yao*

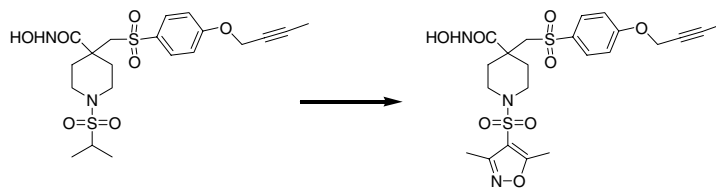


A novel series of potent active-site inhibitors for HCV NS5B polymerase was identified, and the corresponding X-ray structural study was described.

Identification of potent and selective TACE inhibitors via the S1 pocket

pp 34–39

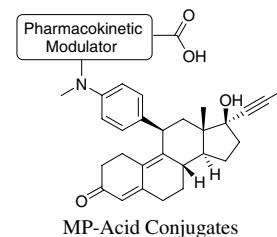
Jeffrey S. Condon, Diane Joseph-McCarthy, Jeremy I. Levin, Henry-Georges Lombart, Frank E. Lovering,*
 Linhong Sun, Weiheng Wang, Weixin Xu and Yuhua Zhang

**Parallel strategies for the preparation and selection of liver-targeted glucocorticoid receptor antagonists**

pp 40–44

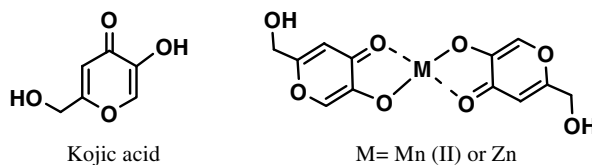
Bradley J. Backes,* Gregory L. Hamilton, Phong Nguyen, Denise Wilcox, Steven Fung, Jiahong Wang,
 Marlena Grynfarb, Annika Goos-Nilsson, Peer B. Jacobson and Thomas W. von Geldern

Libraries of mifepristone analogs, MP-Acids, were shown to be potent GR antagonists in binding and cell-based functional screens. A high-throughput pharmacokinetic selection strategy was devised to identify MP-Acids with liver-targeting profiles. These conjugates were tested in in vivo models to evaluate liver versus systemic GR antagonism.

**Kojic acid and its manganese and zinc complexes as potential radioprotective agents**

pp 45–48

Saeed Emami,* Seyed Jalal Hosseinimehr, Seyed Mohammad Taghdisi and Shahram Akhlaghpour

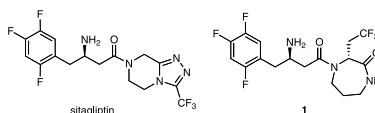


The naturally occurring fungal metabolite kojic acid and its manganese and zinc complexes have been evaluated as potential radioprotectors in mice. Their toxicity and radioprotective activity (survival rate) have been determined and compared with that of WR-2721 (amifostine). The results of in vivo radioprotection showed that these compounds exhibited significant radioprotective effects against lethal dose of γ -irradiation in mice.

(3R)-4-[(3R)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-3-(2,2,2-trifluoroethyl)-1,4-diazepan-2-one, a selective dipeptidyl peptidase IV inhibitor for the treatment of type 2 diabetes

pp 49–52

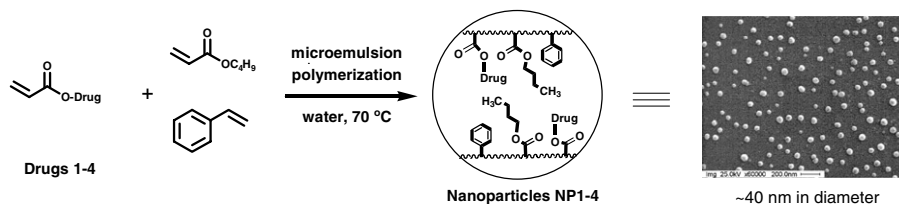
Tesfaye Biftu,* Dennis Feng, Xiaoxia Qian, Gui-Bai Liang, Gerard Kieczkowski, George Eiermann,
 Huaibing He, Barbara Leiting, Kathy Lyons, Aleksandr Petrov, Ranabir Sinha-Roy, Bei Zhang,
 Giovanna Scapin, Sangita Patel, Ying-Duo Gao, Suresh Singh, Joseph Wu, Xiaoping Zhang,
 Nancy A. Thornberry and Ann E. Weber



Replacement of the triazolopiperazine ring of sitagliptin (DPP-4 IC_{50} = 18 nM) with 3-(2,2,2-trifluoroethyl)-1,4-diazepan-2-one gave dipeptidyl peptidase IV (DPP-4) inhibitor **1** which is potent (DPP-4 IC_{50} = 2.6 nM), selective, and efficacious in an oral glucose tolerance test in mice. It was selected for extensive preclinical development as a potential back-up candidate to sitagliptin.

Antibiotic-conjugated polyacrylate nanoparticles: New opportunities for development of anti-MRSA agents pp 53–56

Edward Turos,* Jeung-Yeop Shim, Yang Wang, Kerriann Greenhalgh, G. Suresh Kumar Reddy, Sonja Dickey and Daniel V. Lim

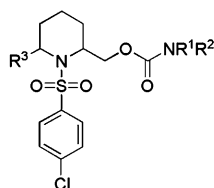


Antibacterially active polyacrylate nanoparticles in the range of 30–50 nm have been synthesized in water by emulsion polymerization of an *N*-thiolated β -lactam acrylate pre-dissolved in a mixture of butyl acrylate and styrene (7:3). The resulting emulsions display potent in vitro activity against MRSA.

**2,6-Disubstituted *N*-arylsulfonyl piperidines as γ -secretase inhibitors**

pp 57–62

Dmitri A. Pissarnitski,* Theodoros Asberom, Thomas A. Bara, Alex V. Buevich, John W. Clader, William J. Greenlee, Henry S. Guzik, Hubert B. Josien, Wei Li, Michael McEwan, Brian A. McKittrick, Terry L. Nechuta, Eric M. Parker, Lisa Sinning, Elizabeth M. Smith, Lixin Song, Henry A. Vaccaro, Johannes H. Voigt, Lili Zhang, Qi Zhang and Zhiqiang Zhao



A novel piperidine series of γ -secretase inhibitors, potentially useful for the treatment of Alzheimer's disease, is disclosed.

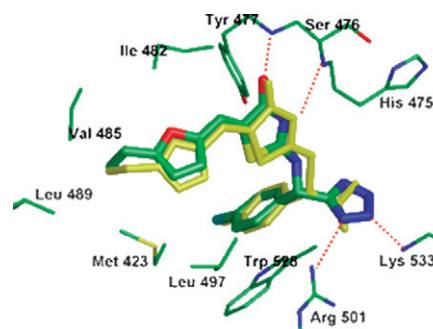
Novel thiazolones as HCV NS5B polymerase allosteric inhibitors:

pp 63–67

Further designs, SAR, and X-ray complex structure

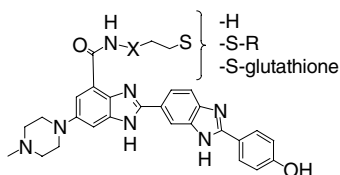
Shunqi Yan,* Gary Larson, Jim Z. Wu, Todd Appleby, Yili Ding, Robert Hamatake, Zhi Hong and Nanhua Yao*

The follow-up designs and more detailed SAR of thiazolone derivatives as novel inhibitors of HCV NS5B polymerase were described. The X-ray complex structure for the new inhibitor was obtained at a resolution of 2.2 Å, and confirmed the design.

**Equilibrium shift by target DNA substrates for determination of DNA binding ligands**

pp 68–72

Saori Tsujita, Mikimasa Tanada, Tomonobu Kataoka and Shigeki Sasaki*



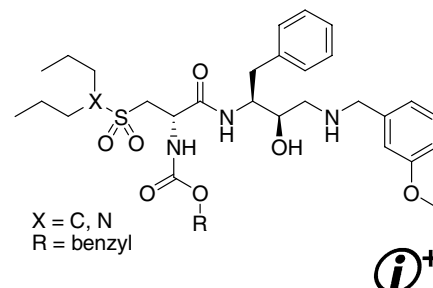
The equilibrium constructed of the Hoechst-thiol and the disulfide derivatives in the presence of glutathione was shifted by the addition of the template DNA to produce higher-affinity compounds.

Design of potent inhibitors of human β -secretase. Part 1

pp 73–77

John N. Freskos,* Yvette M. Fobian, Timothy E. Benson, Michael J. Bienkowski, David L. Brown, Thomas L. Emmons, Robert Heintz, Alice Laborde, Joseph J. McDonald, Brent V. Mischke, John M. Molyneaux, Joseph B. Moon, Patrick B. Mullins, D. Bryan Prince, Donna J. Paddock, Alfredo G. Tomasselli and Gregory Winterrowd

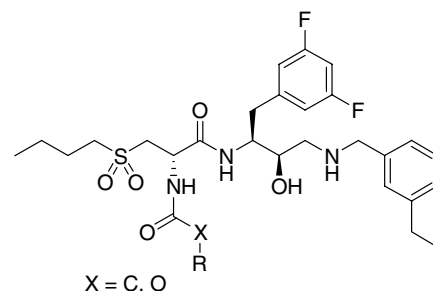
We describe a novel series of potent inhibitors of human β -secretase. These compounds possess the hydroxyethyl amine transition state isostere. A 2.5 Å crystal structure of inhibitor **32** bound to BACE is provided.

**Design of potent inhibitors of human β -secretase. Part 2**

pp 78–81

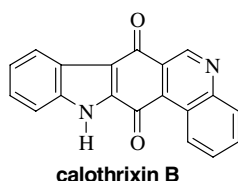
John N. Freskos,* Yvette M. Fobian, Timothy E. Benson, Joseph B. Moon, Michael J. Bienkowski, David L. Brown, Thomas L. Emmons, Robert Heintz, Alice Laborde, Joseph J. McDonald, Brent V. Mischke, John M. Molyneaux, Patrick B. Mullins, D. Bryan Prince, Donna J. Paddock, Alfredo G. Tomasselli and Greg Winterrowd

We describe an optimized series of acyclic hydroxyethylamine transition state isosteres of β -secretase that incorporate a variety of P₂ side chains that yield potent inhibitors with excellent cellular activity and good selectivity against Cathepsin-D.

**Structure–activity delineation of quinones related to the biologically active Calothrixin B**

pp 82–85

Paul H. Bernardo, Christina L. L. Chai,* Maurice Le Guen, Geoffrey D. Smith and Paul Waring



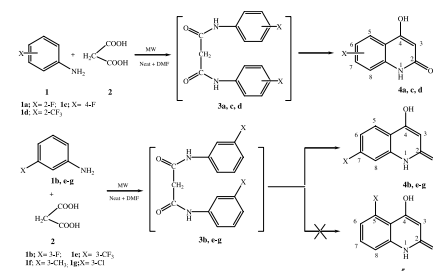
The biological activities of Calothrixin B and six related analogues against three cell lines are reported. The results of the structure–activity relationship study are discussed.

Microwave prompted multigram synthesis, structural determination, and photo-antiproliferative activity of fluorinated 4-hydroxyquinolones

pp 86–93

Kapil Arya* and Manish Agarwal

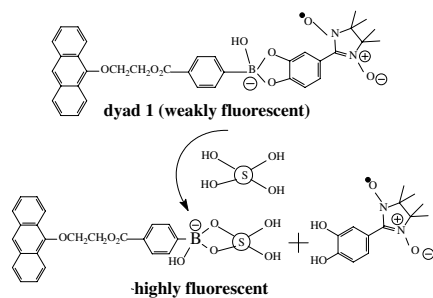
A simple facile one-step microwave enhanced multigram synthesis of such fluorinated quinolones in reasonable purity has been developed in excellent yield (85–94%) in 3–5 min and evaluated for photo-antiproliferative, antimicrobial, and antituberculosis activities.



Formation of the intermediate nitronyl nitroxide–anthracene dyad sensing saccharides

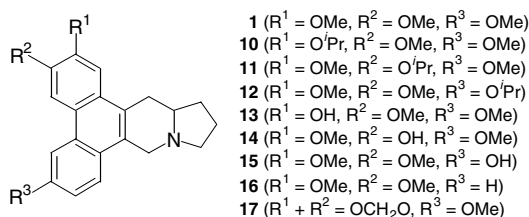
pp 94–96

Yanxin Yu, Deqing Zhang,* Wei Tan, Zhiyong Wang and Daoben Zhu*

**Synthesis and structure–activity studies of antofine analogues as potential anticancer agents**

pp 97–100

Ye Fu, Sang Kook Lee, Hye-Young Min, Taeho Lee, Jaekwang Lee, Maosheng Cheng and Sanghee Kim*

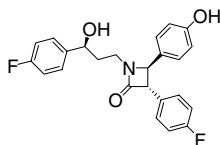


To define the features of the molecule that are essential for cytotoxicity, we have synthesized and evaluated a series of phenanthroindolizidine alkaloid, antofine (**1**), analogues (**10–17**).

Ezetimibe analogs with a reorganized azetidinone ring: Design, synthesis, and evaluation of cholesterol absorption inhibitions

pp 101–104

Xianxiu Xu, Renzhong Fu, Jin Chen, Shengwu Chen and Xu Bai*



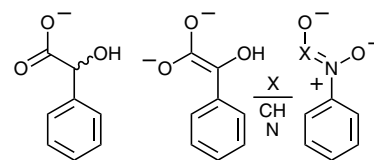
Four individual isomers of backbone re-organized ezetimibe analogs were designed, synthesized, and evaluated for cholesterol absorption inhibition in rats.

Intermediate analogue inhibitors of mandelate racemase: *N*-Hydroxyformanilide and cupferron

pp 105–108

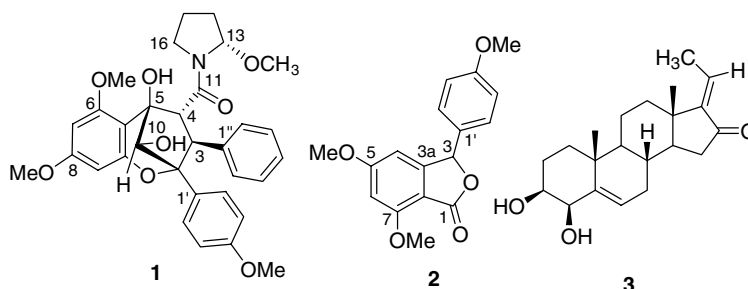
Jennifer R. Bourque, Rodney K. M. Burley and Stephen L. Bearn*

Mandelate racemase (MR) catalyzes the interconversion of the enantiomers of mandelate and has been studied as a paradigm for enzyme-catalyzed proton abstraction from carbon acids. Intermediate analogues *N*-hydroxyformanilide (HFA; X = CH; $K_i = 2.79 \pm 0.19 \mu\text{M}$) and cupferron (X = N; $K_i = 2.67 \pm 0.09 \mu\text{M}$) are identified as potent competitive inhibitors of MR. The pH–p*K_i* profile indicates that MR can bind either the protonated or deprotonated forms of HFA, with a 10-fold greater affinity for the latter form.



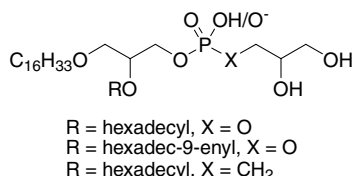
Ponapensin, a cyclopenta[*bc*]benzopyran with potent NF- κ B inhibitory activity from *Aglaia ponapensis* pp 109–112

Angela A. Salim, Alison D. Pawlus, Hee-Byung Chai, Norman R. Farnsworth, A. Douglas Kinghorn and Esperanza J. Carcache-Blanco*

**Synthesis and surface activity of diether-linked phosphoglycerols:
Potential applications for exogenous lung surfactants**

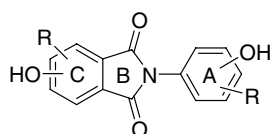
pp 113–117

Robert H. Notter, Zhongyi Wang, Zhengdong Wang, Jason A. Davy and Adrian L. Schwan*

**Estrogen receptor β ligands: Design and synthesis of new 2-phenyl-isoindole-1,3-diones**

pp 118–122

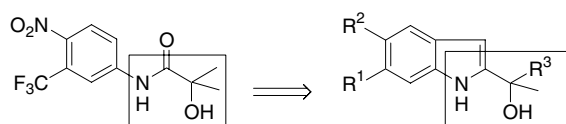
John W. Ullrich,* Rayomand J. Unwalla, Robert R. Singhaus, Jr., Heather A. Harris and Richard E. Mewshaw



The design, synthesis and biological evaluation of the 2-phenyl-isoindole-1,3-diones will be discussed. Detailed modeling studies with X-ray support were used to understand the ligand binding orientation and observed selectivity.

The discovery of a potent orally efficacious indole androgen receptor antagonist through in vivo screening pp 123–126

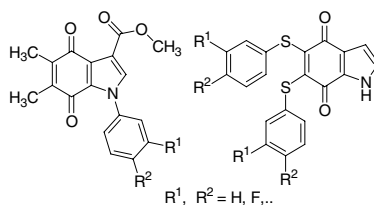
James C. Lanter,* James J. Fiordeliso, Weiqin Jiang, George F. Allan, Muh-Tsann Lai, Olivia Linton, Do Won Hahn, Scott G. Lundeen and Zhihua Sui



Synthesis and antifungal activity of 1*H*-indole-4,7-diones

pp 127–131

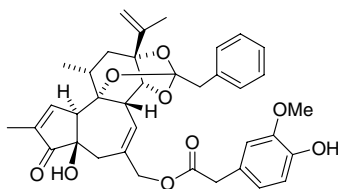
Chung-Kyu Ryu,* Jung Yoon Lee, Rae-Eun Park, Mi-Young Ma and Ji-Hee Nho



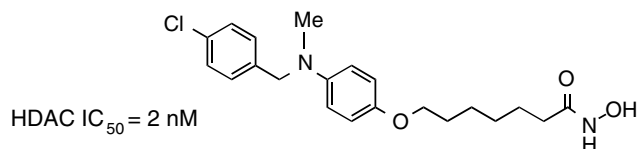
1*H*-Indole-4,7-diones were synthesized and tested for in vitro antifungal activity against fungi. Many of tested them exhibited potent antifungal activity.

Structure–activity relationships of the ultrapotent vanilloid resiniferatoxin (RTX): The homovanillyl moiety pp 132–135

Giovanni Appendino,* Abdellah Ech-Chahad, Alberto Minassi, Sara Bacchiega, Luciano De Petrocellis and Vincenzo Di Marzo*

**Structure–activity relationships of aryloxyalkanoic acid hydroxyamides as potent inhibitors of histone deacetylase** pp 136–141

Charles M. Marson,* Thevaki Mahadevan, Jon Dines, Stéphane Sengmany, James M. Morrell, John P. Alao, Simon P. Joel, David M. Vigushin and R. Charles Coombes

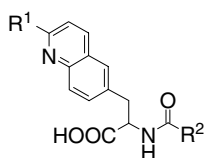


Aryl ether inhibitors of histone deacetylase are described.

2,6-Quinolinylnyl derivatives as potent VLA-4 antagonists

pp 142–146

Marie-Agnès Lassoie, Fabienne Broeders, Philippe Collart, Laurent Defrère, Françoise de Laveleye-Defais, Thierry Demaude, Abdoulaye Gassama, Gérald Guillaumet, Jean-Claude Hayez, Laszlo Kiss, Laurent Knerr, Jean-Marie Nicolas, Stéphanie Norsikian, Luc Quéré, Sylvain Routier, Valérie Verbois and Laurent Provins*

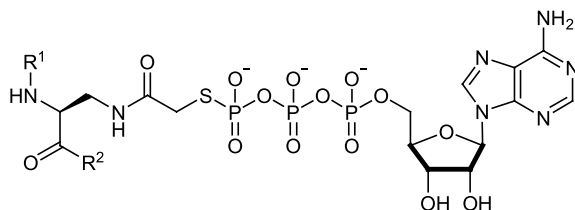


The synthesis and SAR around 2,6-quinolinylnyl derivatives as potent orally bioavailable VLA-4 antagonists is reported.

ATP-conjugated peptide inhibitors for calmodulin-dependent protein kinase II

pp 147–151

Dae-Ro Ahn, Ki-Cheol Han, Hyuk Sung Kwon and Eun Gyeong Yang*

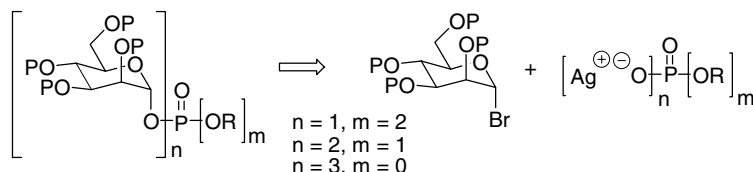


Conjugation of AIP peptide inhibitors to ATP γ S by considering a phosphoryl transfer mechanism led to improved potency in CaMKII (calmodulin-dependent protein kinase II) inhibition, which was ATP-competitive and substrate-uncompetitive.

**Mono, di and tri-mannopyranosyl phosphates as mannose-1-phosphate prodrugs for potential CDG-Ia therapy**

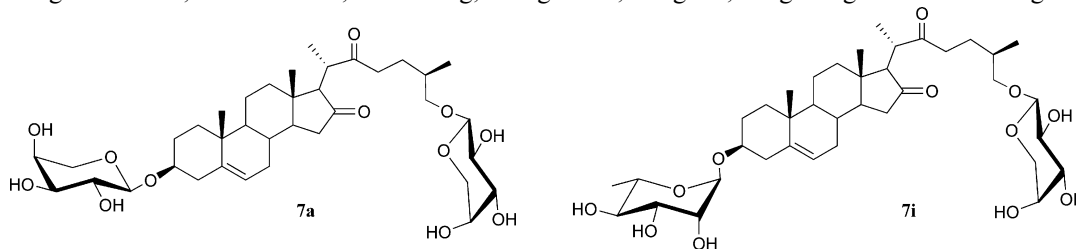
pp 152–155

Renaud Hardré, Amira Khaled, Alexandra Willemetz, Thierry Dupré, Stuart Moore, Christine Gravier-Pelletier* and Yves Le Merrer*

**Synthesis of bisdesmosidic kryptogenyl saponins using the 'random glycosylation' strategy and evaluation of their antitumor activity**

pp 156–160

Yang Liu, Dong-Mei Zhao, Xue-Hua Lu, Hui Wang, Hong Chen, Ying Ke, Ling Leng and Mao-Sheng Cheng*

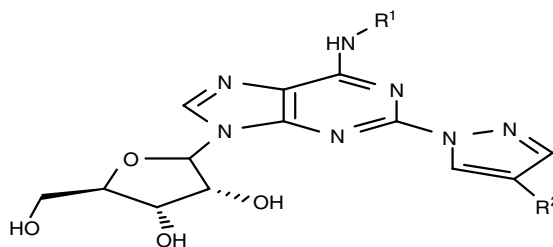


A library of 16 novel bisdesmosidic kryptogenyl saponins was built for investigation of antitumor activity, wherein two compounds showed inhibition against HeLa cells ($IC_{50} = 4.25 \mu M$ for **7a** and $8.36 \mu M$ for **7i**).

N⁶-Cycloalkyl-2-substituted adenosine derivatives as selective, high affinity adenosine A₁ receptor agonists

pp 161–166

Elfatih Elzein,* Rao Kalla, Xiaofen Li, Thao Perry, Tim Marquart, Mark Micklatcher, Yuan Li, Yuzhi Wu, Dewan Zeng and Jeff Zablocki



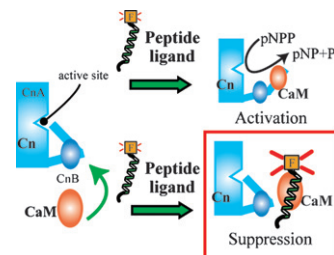
The synthesis, binding affinity and selectivity of 2,6-disubstituted adenosine derivatives for the A₁-AdoR is reported.

Screening of α -helical peptide ligands controlling a calcineurin-phosphatase activity

pp 167–171

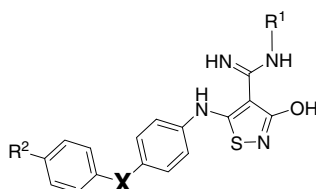
Kenji Usui, Kin-ya Tomizaki and Hisakazu Mihara*

Demonstrated was the application of screening for peptide ligands that tightly bind to a target protein and also control the protein's functions. The strategy using a designed peptide library shows real promise as a peptide-based novel screening system.

**Identification of novel, selective and potent Chk2 inhibitors**

pp 172–175

Gary Larson, Shunqi Yan, Huanming Chen, Frank Rong, Zhi Hong and Jim Zhen Wu*

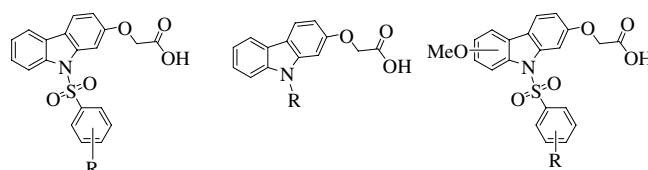


Novel, selective and potent Chk2 inhibitors were identified. Their SAR and computer modeling studies were conducted.

***N*-Substituted carbazolyloxyacetic acids modulate Alzheimer associated γ -secretase**

pp 176–182

Rajeshwar Narlawar, Blanca I. Pérez Revuelta, Karlheinz Baumann, Robert Schubel, Christian Haass, Harald Steiner and Boris Schmidt*



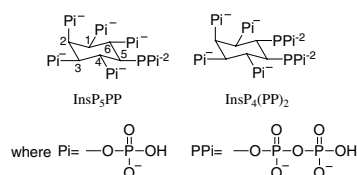
N-Sulfonylated and *N*-alkylated carbazolyloxyacetic acids were investigated for the inhibition and modulation of the Alzheimer's disease associated γ -secretase. The most active compounds displayed activity on amyloid precursor protein (APP) overexpressing cell lines in the low micromolar range and little or no effect on the γ -secretase cleavage at the ϵ -site.

Phosphate transfer from inositol pyrophosphates InsP_5PP and $\text{InsP}_4(\text{PP})_2$:

pp 183–188

A semi-empirical investigation

Christine E. Hand and John F. Honek*



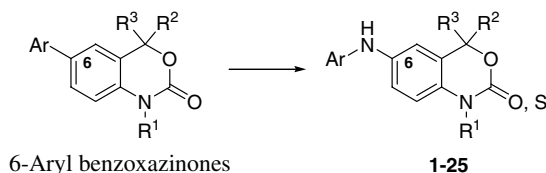
PM3/SM5.2 semi-empirical calculations were used to calculate the free energy of phosphate transfer from InsP_5PP and $\text{InsP}_4(\text{PP})_2$ to methanol as a model system for non-enzymatic phosphorylation of protein residues by these intracellular pyrophosphates.



SAR studies of 6-(arylamino)-4,4-disubstituted-1-methyl-1,4-dihydro-benzo[d][1,3]oxazin-2-ones as progesterone receptor antagonists

pp 189–192

Jeffrey C. Kern, Eugene A. Terefenko, Andrew Fensome, Ray Unwalla, Jay Wrobel, Yuan Zhu, Jeffrey Cohen, Richard Winneker, Zhiming Zhang and Puwen Zhang*

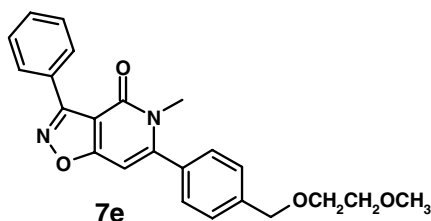


Insertion of a NH linker at the 6-position of 6-aryl benzoxazinones, the progesterone receptor (PR) modulators, led to exclusively PR antagonists (**1–25**) in a progesterone induced alkaline phosphatase assay in the T47D cells.

Identification of a series of highly potent activators of the Nurrl signaling pathway

pp 193–196

Samuel Hintermann,* Michele Chiesi, Ulrike von Krosigk, Danièle Mathé, Richard Felber and Bastian Hengerer



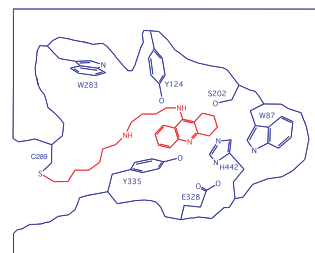
Hit identification and SAR studies leading to the isoxazolo-pyridinone **7e**, a highly potent, brain penetrable activator of the Nurrl signaling pathway, are described.

Species marker for developing novel and safe pesticides

pp 197–199

Yuan-Ping Pang*

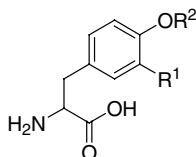
Current anticholinesterase pesticides are toxic to mammals as they target a catalytic serine residue of acetylcholinesterases (AChEs) in insects and in mammals. This article reports a cysteine residue present at the active sites of greenbug and aphid AChEs but absent at those of mammalian AChEs. This discovery enables the design of novel and safe pesticides that target the cysteine residue rather than the ubiquitous serine residue.



Syntheses of F-18 labeled fluoroalkyltyrosine derivatives and their biological evaluation in rat bearing 9L tumor

pp 200–204

Byung Seok Moon, Tae Sup Lee, Kyo Chul Lee, Gwang Il An, Gi Jeong Cheon, Sang Moo Lim, Chang Woon Choi, Dae Yoon Chi and Kwon Soo Chun*



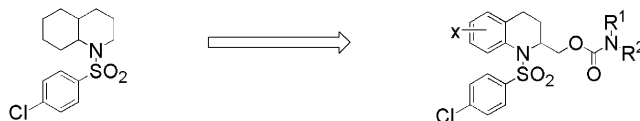
- 1, R¹ = CH₂CH₂F, R² = H
- 2, R¹ = CH₂CH₂CH₂F, R² = H
- 3, R¹ = CH₂CH₂F, R² = CH₃
- 4, R¹ = CH₂CH₂CH₂F, R² = CH₃

The syntheses of F-18 labeled fluoroalkyltyrosine derivatives and their biological evaluation are reported.

Tetrahydroquinoline sulfonamides as γ -secretase inhibitors

pp 205–207

Theodros Asberom,* Thomas A. Bara, John W. Clader, William J. Greenlee,
Henry S. Guzik, Hubert B. Josien, Wei Li, Eric M. Parker,
Dmitri A. Pissarnitski, Lixin Song, Lili Zhang and Zhiqiang Zhao

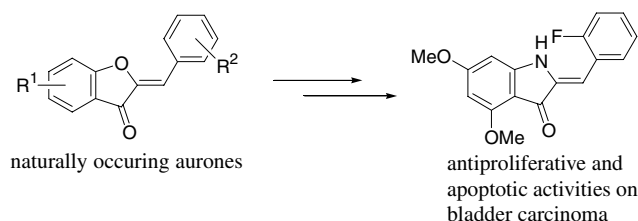


The development of a novel series of tetrahydroquinoline-derived γ -secretase inhibitors for the potential treatment of Alzheimer's disease is described.

2-Arylidenedihydroindole-3-ones: Design, synthesis, and biological activity on bladder carcinoma cell lines

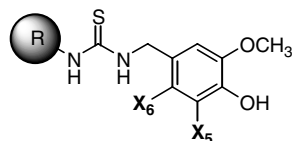
pp 208–213

Bastien Gerby, Ahcène Boumendjel,* Madeleine Blanc, Pierre Paul Bringuier,
Pierre Champelovier, Antoine Fortuné, Xavier Ronot and Jean Boutonnat

**Halogenation of 4-hydroxy-3-methoxybenzyl thiourea TRPV1 agonists showed enhanced antagonism to capsaicin**

pp 214–219

Dong Wook Kang, HyungChul Ryu, Jeewoo Lee,* Krystle A. Lang, Vladimir A. Pavlyukovets,
Larry V. Pearce, Tetsuro Ikeda, Jozsef Lazar and Peter M. Blumberg

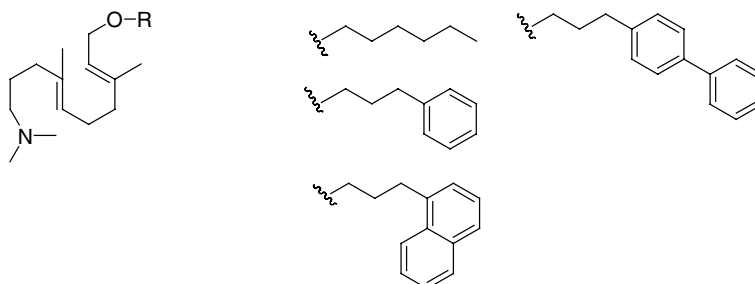


Selected potent TRPV1 agonists have been modified by 5- or 6-halogenation on the aromatic A-region to analyze their effects on potency and efficacy (agonism versus antagonism).

Design, synthesis, and biological evaluation of new (2*E*,6*E*)-10-(dimethylamino)-3,7-dimethyl-2,6-decadien-1-ol ethers as inhibitors of human and *Trypanosoma cruzi* oxidosqualene cyclase

pp 220–224

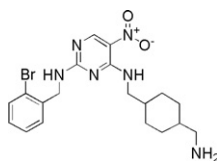
Ubalda Galli,* Simonetta Oliaro-Bosso, Silvia Taramino, Serena Venegoni, Emanuele Pastore,
Gian Cesare Tron, Gianni Balliano, Franca Viola* and Giovanni Sorba



Discovery of potent and selective PKC- θ inhibitors

pp 225–230

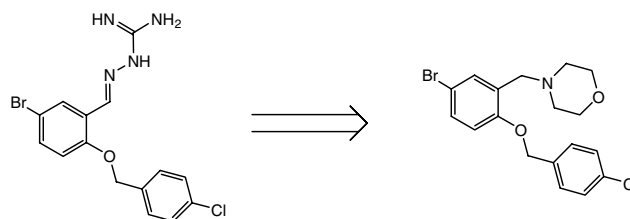
Charles L. Cywin,* Georg Dahmann, Anthony S. Prokopowicz, III, Erick R. R. Young, Ronald L. Magolda, Mario G. Cardozo, Derek A. Cogan, Darren DiSalvo, John D. Ginn, Mohammed A. Kashem, John P. Wolak, Carol A. Homon, Thomas M. Farrell, Heather Grbic, Hanbo Hu, Paul V. Kaplita, Lisa H. Liu, Denice M. Spero, Deborah D. Jeanfavre, Kathy M. O'Shea, Della M. White, Joseph R. Woska, Jr., and Maryanne L. Brown

**CCR5 receptor antagonists: Discovery and SAR study of guanyldiazide derivatives**

pp 231–234

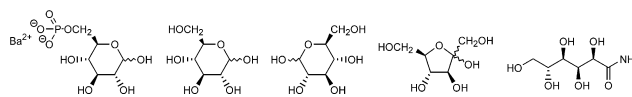
Robert G. Wei,* Damian O. Arnaiz, Yuo-Ling Chou, Dave Davey, Laura Dunning, Wheeseong Lee, Shou-Fu Lu, James Onuffer, Bin Ye and Gary Phillips

High throughput screening (HTS) led to the identification of the guanyldiazide of 2-(4-chlorobenzoyloxy)-5-bromobenzaldehyde as a CCR5 receptor antagonist. Modifications of the guanyldiazide resulted in the discovery of novel CCR5 antagonists.

**Glucose-specific poly(allylamine) hydrogels—A reassessment**

pp 235–238

Furqan M. Fazal and David E. Hansen*

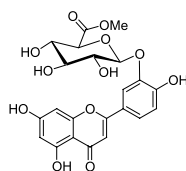


Polymer hydrogels synthesized from poly(allylamine hydrochloride) crosslinked in the presence of D-glucose-6-phosphate monobarium salt do not show imprinting on the molecular level—rather, the differential solubilities of carbohydrate analytes in the bulk polymer account for the binding data observed.

New antifungal flavonoid glycoside from *Vitex negundo*

pp 239–242

B. Sathiamoorthy, Prasoon Gupta, Manmeet Kumar, Ashok K. Chaturvedi, P. K. Shukla and Rakesh Maurya*



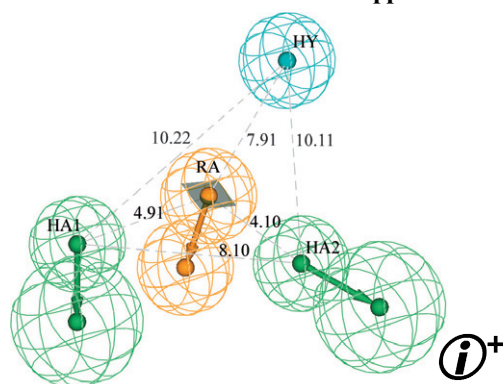
New flavone glycoside was isolated along with five known compounds from the leaves of *Vitex negundo* and evaluated for their antifungal and antibacterial activity. The new flavone glycoside was found to have significant antifungal activity against *Trichophyton mentagrophytes* and *Cryptococcus neoformans* at MIC 6.25 μ g/ml using flucanazole as standard drug.

Farnesyltransferase pharmacophore model derived from diverse classes of inhibitors

pp 243–249

Aijun Lu, Jian Zhang, Xiaojin Yin, Xiaomin Luo and Hualiang Jiang*

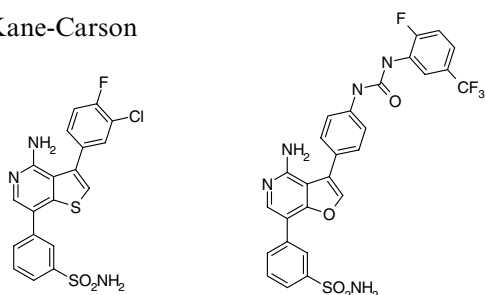
The best pharmacophore model produced in Catalyst 4.10 by 25 farnesyltransferase inhibitors in training set. It consists of four features, two hydrogen-bond acceptors (HA), one hydrophobic point (HY), and one ring aromatic feature (RA).

**Design and effective synthesis of novel templates, 3,7-diphenyl-4-amino-thieno and furo-[3,2-c]pyridines as protein kinase inhibitors and in vitro evaluation targeting angiogenic kinases**

pp 250–254

Yasushi Miyazaki,* Masato Nakano, Hideyuki Sato, Anne T. Truesdale, J. Darren Stuart, Eldridge N. Nartey, Kendra E. Hightower and Laurie Kane-Carson

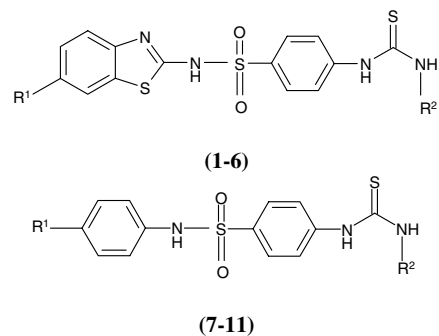
A novel class of 3,7-diphenyl-4-amino-thieno and furo[3,2-c]pyridine has been designed based on pharmacophore models of ATP competitive kinase inhibitors. Versatile synthetic methods via double Suzuki coupling to explore SAR have been established and potent inhibitors against angiogenic target, VEGFR2, Tie2, and EphB4, have been successfully discovered.

**Synthesis and anticonvulsant activity of sulfonamide derivatives-hydrophobic domain**

pp 255–259

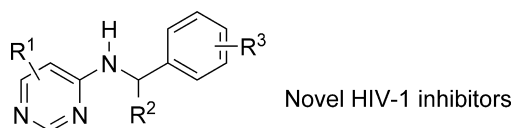
Nadeem Siddiqui,* Surendra N. Pandeya, Suroor A. Khan, James Stables, Arpana Rana, Mahfuz Alam, Md. Faiz Arshad and Mashooq A. Bhat

N-(6-‘substituted’-1,3-benzothiazol-2-yl)-4-[(‘substituted’ amino) carbonothionyl] amino} benzenesulfonamides (**1–6**) and *N*-(4-‘substituted’ phenyl)-4-[(‘substituted’ amino carbonothionyl] amino} benzenesulfonamides (**7–11**) were synthesized and evaluated for their possible anticonvulsant, neurotoxic studies and their potential hydrophobic domain has been described.

**4-Aminopyrimidines as novel HIV-1 inhibitors**

pp 260–265

Venkat R. Gadachanda, Baogen Wu, Zhiwei Wang, Kelli L. Kuhen, Jeremy Caldwell, Helmut Zondler, Harald Walter, Mark Havenhand and Yun He*

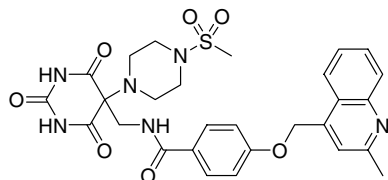


Novel HIV-1 inhibitors

Discovery of low nanomolar non-hydroxamate inhibitors of tumor necrosis factor- α converting enzyme (TACE)

pp 266–271

James J.-W. Duan,* Lihua Chen, Zhonghui Lu, Bin Jiang, Naoyuki Asakawa, James E. Sheppeck, Rui-Qin Liu, Maryanne B. Covington, William Pitts, Soong-Hoon Kim and Carl P. Decicco

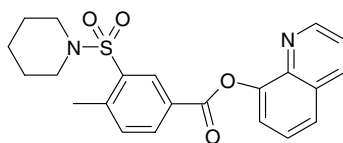


Compound 51
pTACE (IC₅₀): 0.002 μ M

Arylsulfonamides as a new class of cannabinoid CB₁ receptor ligands: Identification of a lead and initial SAR studies

pp 272–277

N. Lambeng, F. Lebon, B. Christophe, M. Burton, M. De Ryck and L. Quéré*



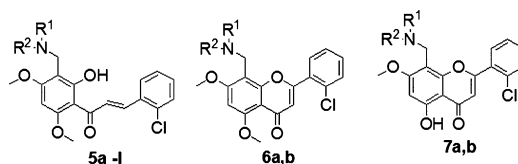
Compound 1

High-throughput screening identified the piperidinyl-sulfonyl benzoic ester **1** as a novel agonist for CB₁ receptor with nanomolar affinity. We report here the pharmacological profile of compound **1** as well as preliminary biological activities in pain model. Analogs were purchased and the structure–affinity relationships among this novel class are discussed.

Nitrogen-containing flavonoids as CDK1/Cyclin B inhibitors: Design, synthesis, and biological evaluation

pp 278–281

Tao Liu, Zhongmiao Xu, Qiaojun He, Yanhong Chen, Bo Yang and Yongzhou Hu*

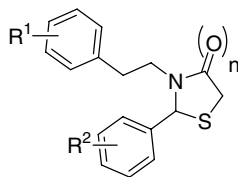


A novel series of nitrogen-containing flavonoids **5a–l**, **6a,b**, and **7a,b** were designed and synthesized as cyclin-dependent kinases inhibitors. The representative compounds **5a**, **5b**, **5e**, and **5g** showed potent CDK1/Cyclin B inhibitory activities.

Evolution of thiazolidine-based blockers of human Kv1.5 for the treatment of atrial arrhythmias

pp 282–284


Chris M. Jackson, Benjamin Blass, Keith Coburn, Laurent Djandjighian, Gina Fadaye, Andrew J. Fluxe, Steven J. Hodson, John M. Janusz,* Michael Murawsky, James M. Ridgeway, Ronald E. White and Shengde Wu



The synthesis and evaluation of a series of thiazolidine based blockers of human Kv1.5 is described.

OTHER CONTENTS**Summary of instructions to authors****p I**

*Corresponding author

 Supplementary data available via ScienceDirect**COVER**

Typical snapshot of **7b** bound to HIV-RT from an MC simulation. Carbon atoms of **7b** are gold; from the left, Tyr181, Tyr188, Phe227, Leu100, Lys101; Trp229 at the top, Val106 at the bottom. H-bond with Lys101 O on right. Some residues in front including Glu138 have been removed for clarity. The water on N5 is also H-bonded to a carboxylate O of Glu138. [Thakur, V. T.; Kim, J. T.; Hamilton, A. D.; Bailey, C. M.; Domaoal, R. A.; Wang, L.; Anderson, K. S.; Jorgensen, W. L. *Bioorg. Med. Chem. Lett.* **2006**, 16, 5664.]

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