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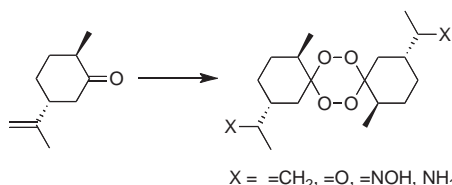
Contents

REGULAR ARTICLES

The structure and antimalarial activity of dispiro-1,2,4,5-tetraoxanes derived from (+)-dihydrocarvone

pp 6359–6361

Yuxiang Dong, Kevin J. McCullough, Sergio Wittlin, Jacques Chollet, Jonathan L. Vennerstrom*



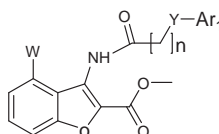
The synthesis, structure elucidation, and antimalarial activity of dispiro-1,2,4,5-tetraoxanes derived from (+)-dihydrocarvone are described.



Synthesis and biological evaluation of 3-substituted-benzofuran-2-carboxylic esters as a novel class of ischemic cell death inhibitors

pp 6362–6365

Jeehee Suh*, Kyu Yang Yi, Yun-Suk Lee, Eunhee Kim, Eul Kgun Yum, Sung-eun Yoo



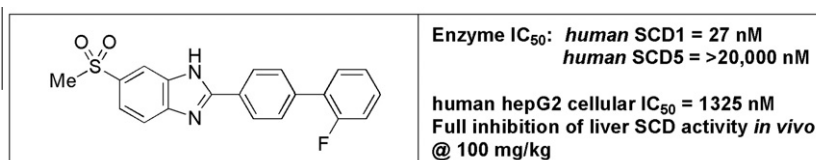
The synthesis and biological evaluation of 3-substituted-benzofuran-2-carboxylic esters are described as an ischemic cell death inhibitors in H9c2 cells and rat primary cardiac myocytes under conditions of oxygen and glucose deprivation.



2-Aryl benzimidazoles: Human SCD1-specific stearyl coenzyme-A desaturase inhibitors

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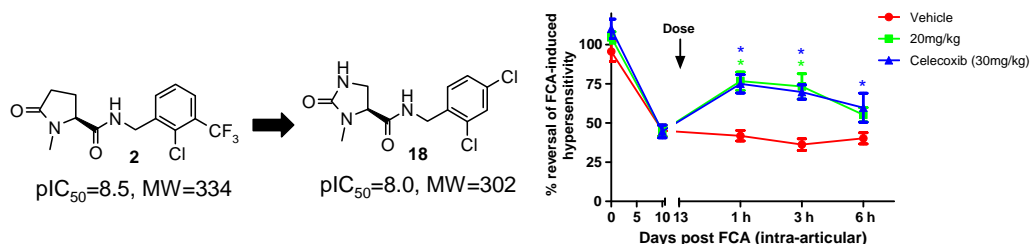
David A. Powell*, Yeeman Ramtohul, Marie-Eve Lebrun, Renata Oballa, Sathesh Bhat, Jean-Pierre Falgueyret, Sebastien Guiral, Zheng Huang, Kathryn Skorey, Paul Tawa, Lei Zhang



Identification of 2-oxo-N-(phenylmethyl)-4-imidazolidinecarboxamide antagonists of the P2X₇ receptor

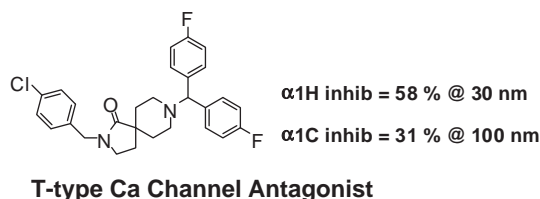
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Lee Abberley, Aude Bebius, Paul J. Beswick, Andy Billinton, Katharine L. Collis, David K. Dean, Elena Fonfria, Robert J. Gleave, Stephen J. Medhurst, Anton D. Michel, Andrew P. Moses, Sadhana Patel, Shilina A. Roman, Tiziana Scoccitti, Beverley Smith, Jon G. A. Steadman, Daryl S. Walter*

**Design, syntheses, and SAR of 2,8-diazaspiro[4.5]decanones as T-type calcium channel antagonists**

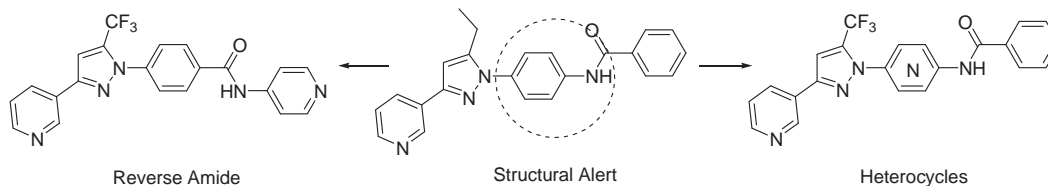
pp 6375–6378

Paul C. Fritch*, Jeffrey Krajewski

**Substituted pyrazoles as novel sEH antagonist: Investigation of key binding interactions within the catalytic domain**

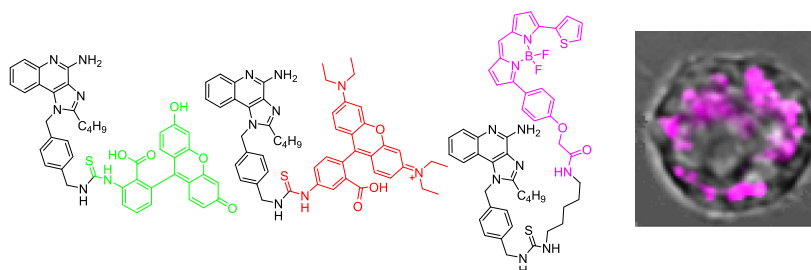
pp 6379–6383

Ho Yin Lo*, Chuk C. Man, Roman W. Fleck, Neil A. Farrow, Richard H. Ingraham, Alison Kukulka, John R. Proudfoot, Raj Betageri, Tom Kirrane, Usha Patel, Rajiv Sharma, Mary Ann Hoermann, Alisa Kabcenell, Stéphane De Lombaert

**Syntheses of fluorescent imidazoquinoline conjugates as probes of Toll-like receptor 7**

pp 6384–6386

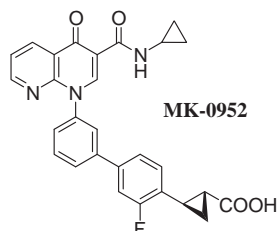
Nikunj M. Shukla, Cole A. Mutz, Rehman Ukani, Hemamali J. Warshakoon, David S. Moore, Sunil A. David*



Discovery of MK-0952, a selective PDE4 inhibitor for the treatment of long-term memory loss and mild cognitive impairment

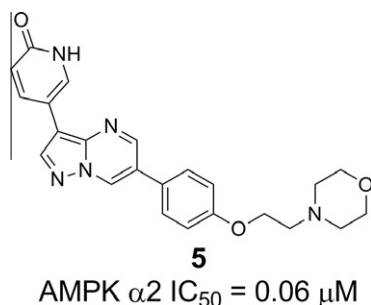
pp 6387–6393

Michel Gallant*, Renee Aspiotis, Stephen Day, Rebecca Dias, Daniel Dubé, Laurence Dubé, Richard W. Friesen, Mario Girard, Daniel Guay, Pierre Hamel, Zheng Huang, Patrick Lacombe, Sebastien Laliberté, Jean-François Lévesque, Susana Liu, Dwight Macdonald, Joseph Mancini, Donald W. Nicholson, Angela Styhler, Karen Townson, Kerry Waters, Robert N. Young, Yves Girard

**The rational design of a novel potent analogue of the 5'-AMP-activated protein kinase inhibitor compound C with improved selectivity and cellular activity**

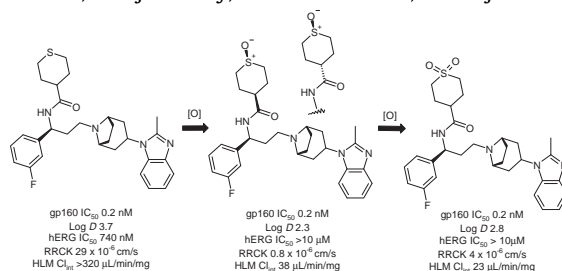
pp 6394–6399

Fouzia Machrouhi, Nouara Ouhamou, Keith Laderoute, Joy Calaoagan, Marina Bukhtiyarova, Paula J. Ehrlich, Anthony E. Klon*

**An in situ oxidation strategy towards overcoming hERG affinity**

pp 6400–6404

David C. Pryde*, Rhys Jones, Donald S. Middleton, Ben J. Laverty, David R. Fenwick, Helen J. Mason, Martin Corless, Nick N. Smith

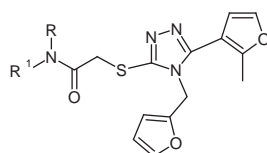


A series of oxidised, for example, sulfoxide, CCR5 antagonists have been identified as highly potent with a large window over inhibition of the hERG channel, but with very low permeability and in vivo absorption. A strategy is described which involved dosing to rats a much more permeable sulfide precursor, which underwent in situ oxidation to the corresponding sulfoxide and sulfone. SAR, metabolism and pharmacokinetic data which underpinned this strategy is described.

2-Methyl-3-furanyl-4H-1,2,4-triazol-3-ylthioamides: A new class of selective orexin 2 antagonists

pp 6405–6407

Fabrizio Micheli*, Marinella Antolini, Romano Di Fabio, Annalisa Pellacani, Alfonso Pozzan

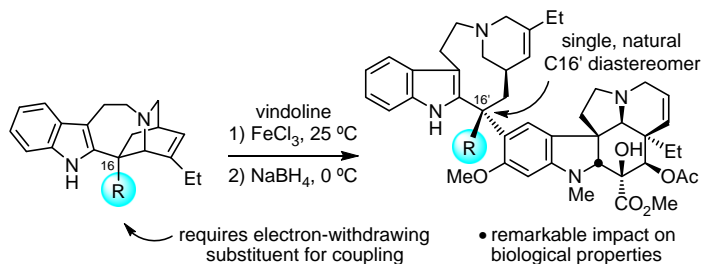


A new class of selective orexin 2 antagonist was identified among commercial products. Initial SAR obtained using commercial derivatives only is presented.

Catharanthine C16 substituent effects on the biomimetic coupling with vindoline: Preparation and evaluation of a key series of vinblastine analogues

pp 6408–6410

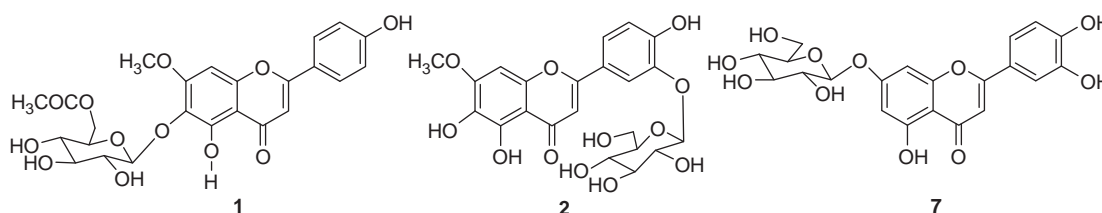
Annie Tam, Hiroaki Gotoh, William M. Robertson, Dale L. Boger*



Flavonoids from *Dracocephalum tanguticum* and their cardioprotective effects against doxorubicin-induced toxicity in H9c2 cells

pp 6411–6415

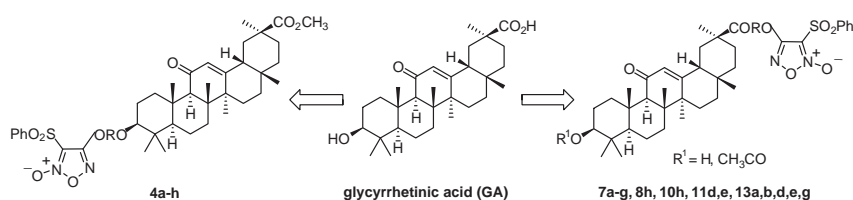
Shu-Qi Wang, Xiu-Zhen Han, Xia Li, Dong-Mei Ren, Xiao-Ning Wang, Hong-Xiang Lou*



Synthesis and biological evaluation of furoxan-based nitric oxide-releasing derivatives of glycyrrhetic acid as anti-hepatocellular carcinoma agents

pp 6416–6420

Yisheng Lai*, Lihong Shen, Zhenzhen Zhang, Wenqing Liu, Yihua Zhang, Hui Ji*, Jide Tian

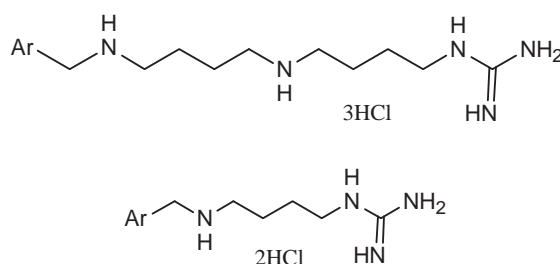


A series of novel furoxan-based nitric oxide (NO)-releasing derivatives of glycyrrhetic acid were synthesized and evaluated for their cytotoxicity against human hepatocellular carcinoma (HCC) cells and NO-releasing ability. Five hybrids displayed selective cytotoxicity against HCC cells with a little effect on the growth of LO2 cells.

Synthesis and bioevaluation of aryl-guanidino polyamine conjugates targeting the polyamine transporter

pp 6421–6425

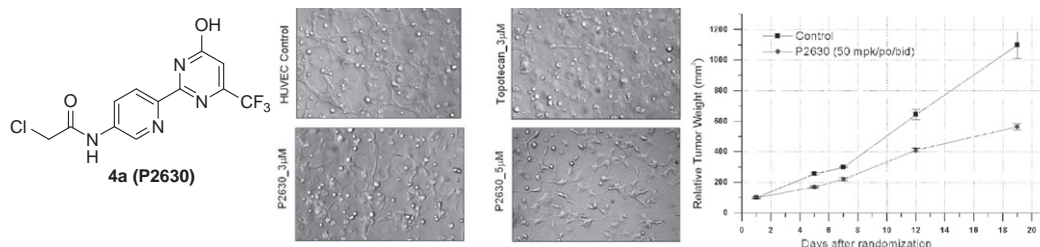
Jianhong Wang, Zhiyong Chen, Songqiang Xie*, Jin Zhao, Chaojie Wang*



Development of novel inhibitors targeting HIF-1 α towards anticancer drug discovery

pp 6426–6429

Nilambari Yewalkar, Vijaykumar Deore, Amol Padgaonkar, Sonal Manohar, Bichismita Sahu, Pramod Kumar, Archana Jalota-Badhwar, Kalpana S. Joshi, Somesh Sharma, Sanjay Kumar*

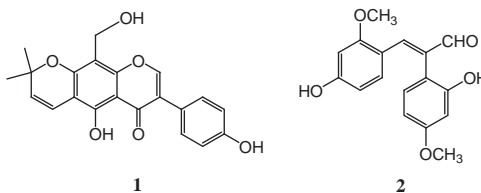


Systemic application of compound P2630, a novel HIF-1 α inhibitor, significantly suppresses the cell proliferation angiogenesis. P2630 has been shown orally efficacious in PC-3 xenograft mice model.

New stilbenoid with inhibitory activity on viral neuraminidases from *Erythrina addisoniae*

pp 6430–6434

Phi Hung Nguyen, MinKyun Na, Trong Tuan Dao, Derek Tantoh Ndinteh, Joseph Tanyi Mbafor, Jaeyoung Park, Hyeonsook Cheong, Won Keun Oh*

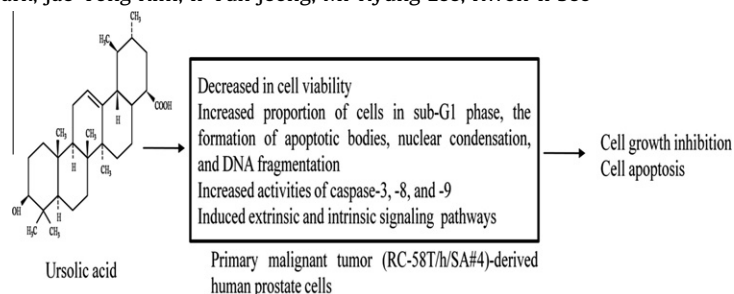


Two new compounds (1 and 2) along with seven known flavonoid derivatives (3–9) were isolated as active principles from an EtOAc-soluble extract of the root bark of *Erythrina addisoniae*. All the isolated compounds (1–9) were tested for their inhibitory activities against both influenza neuraminidases from influenza H1N1 and H9N2. Compound 2, which is a formylated stilbenoid derivative, exhibited strong inhibition of both influenza H1N1 and H9N2 neuraminidases with IC₅₀ values of 8.80 \pm 0.34 μ g/mL and 7.19 \pm 0.40 μ g/mL, respectively.

**Apoptotic action of ursolic acid isolated from *Corni fructus* in RC-58T/h/SA#4 primary human prostate cancer cells**

pp 6435–6438

Seong-Hyuk Kwon, Hye-Young Park, Jae-Yong Kim, Il-Yun Jeong, Mi-Kyung Lee, Kwon-Il Seo*



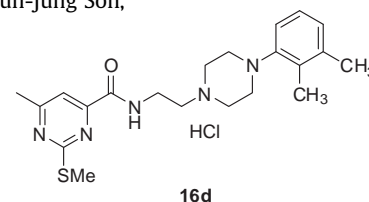
Ursolic acid from *Corni fructus* activated apoptosis in RC-58T/h/SA#4 cells via both caspase-dependent and -independent pathways.

Aryl piperazine-containing pyrimidine 4-carboxamide derivatives targeting serotonin 5-HT_{2A}, 5-HT_{2C}, and the serotonin transporter as a potential antidepressant

pp 6439–6442

Jong Yup Kim, Deukjoon Kim*, Suk Youn Kang, Woo-Kyu Park, Hyun Jung Kim, Myung Eun Jung, Eun-Jung Son, Ae Nim Pae, Jeongmin Kim, Jinhwa Lee*

Aryl piperazine-containing pyrimidine 4-carboxamide derivatives were synthesized and evaluated as novel antidepressant compounds. The various analogues were prepared and bio-assayed for binding to 5-HT_{2A}, 5-HT_{2C} receptor, serotonin transporter. Based on the outcomes of in vitro SAR studies, forced swimming test along with locomotor activities, 16d was identified as a lead compound.



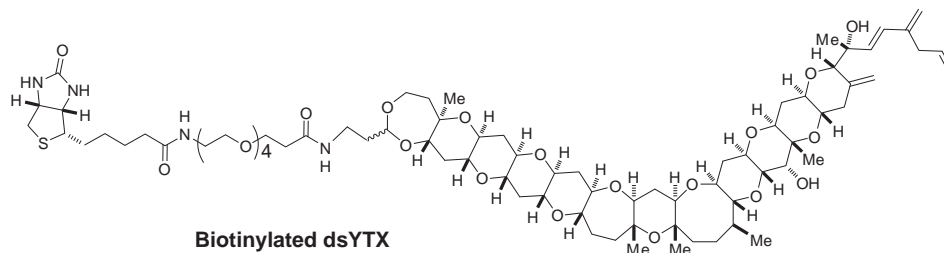
5-HT_{2A} = 47 nM
5-HT_{2C} = 148 nM
SERT = 1014 nM



Detection of Rap1A as a yessotoxin binding protein from blood cell membranes

pp 6443–6446

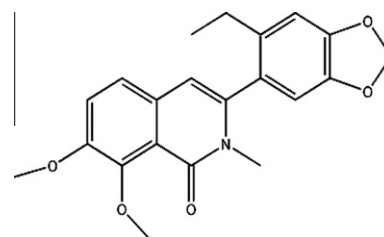
Satoru Ujihara, Tohru Oishi*, Ryota Mouri, Rie Tamate, Keiichi Konoki, Nobuaki Matsumori, Michio Murata*, Yasukatsu Oshima, Naoyuki Sugiyama*, Masaru Tomita, Yasushi Ishihama

**CWJ-081, a novel 3-arylisoquinoline derivative, induces apoptosis in human leukemia HL-60 cells partially involves reactive oxygen species through c-Jun NH₂-terminal kinase pathway**

pp 6447–6451

So-Jung Won, Kyung-Sook Chung, Yo Sook Ki, Jung-Hye Choi, Won-Jea Cho, Kyung-Tae Lee*

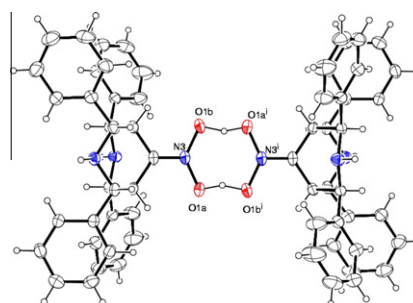
In the present study, we investigated the effect of a novel 3-arylisoquinoline derivative 3-(6-ethyl-benzo[1,3]dioxol-5-yl)-7,8-dimethoxy-2-methyl-2H-isoquinolin-1-one (CWJ-081) on the induction of apoptosis and the putative molecular mechanism of its action in human leukemia cells. Treatment with CWJ-081 exhibited a characteristic feature of apoptosis including externalization of phosphatidylserine and formation of DNA fragmentation in human leukemia cell lines (HL-60, U-937, K-562). In addition, stimulation of HL-60 cells with CWJ-081 induced a series of intracellular events: (1) the activations of caspase-8, -9, and -3; (2) the cleavage of poly (ADP-ribose) polymerase-1 (PARP-1); (3) the loss of mitochondrial membrane potential ($\Delta\psi_m$); (4) the release of cytochrome c; and (5) the modulation of Bcl-2 family proteins. We further demonstrated that CWJ-081 induces reactive oxygen species (ROS) production and c-Jun NH₂-terminal kinase (JNK) activation. Pretreatment with the antioxidant *N*-acetyl-L-cysteine (NAC) markedly inhibited the CWJ-081-induced JNK activation and apoptosis. Moreover, CWJ-081-induced apoptosis was suppressed in the presence of SP600125, a specific JNK inhibitor. Taken together, these data suggest that CWJ-081 induces apoptosis via the mitochondrial apoptotic pathway in HL-60 cells, and ROS-mediated JNK activation plays a key role in the CWJ-081-induced apoptosis.

**Stereocontrolled facile synthesis and antimicrobial activity of oximes and oxime ethers of diversely substituted bispidines**

pp 6452–6458

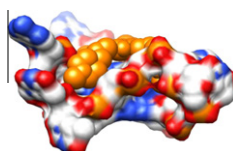
Paramasivam Parthiban, Senthamaraikannan Kabilan, Venkatachalam Ramkumar, Yeon Tae Jeong*

A small library of diversely substituted bispidines and their oximes/oxime ethers viz, 2,4,6,8-tetraaryl-3,7-diazabicyclo[3.3.1]nonan-9-ones and 2,4,6,8-tetraaryl-3,7-diazabicyclo[3.3.1]nonan-9-one oximes/O-methyloximes were synthesized and unambiguously characterized by 1D/2D NMR and single-crystal XRD data. All the synthesized oximes and oxime ethers were tested against a panel of pathogenic bacteria and fungi for their in vitro antibacterial and antifungal activities.

**Tetrasubstituted naphthalene diimide ligands with selectivity for telomeric G-quadruplexes and cancer cells**

pp 6459–6463

Sonja M. Hampel, Assitan Sidibe, Mekala Gunaratnam, Jean-François Riou, Stephen Neidle*



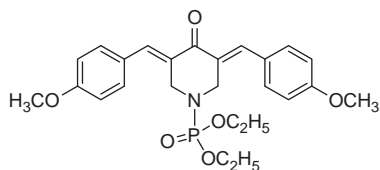
Modelled structure of a naphthalene diimide derivative with four *N*-methylpiperazine end-groups, bound to a parallel form of the human intramolecular telomeric G-quadruplex.



Sequential cytotoxicity: A theory examined using a series of 3,5-bis(benzylidene)-1-diethylphosphono-4-oxopiperidines and related phosphonic acids

pp 6464–6468

Swagatika Das, Umashankar Das, Hiroshi Sakagami, Ken Hashimoto, Masami Kawase, Dennis K. J. Gorecki, Jonathan R. Dimmock*

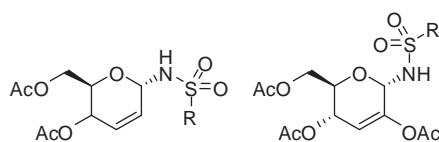


Diethyl ((3*E*,5*E*)-3,5-bis(4-methoxybenzylidene)-4-oxopiperidin-1-yl)phosphonate emerged as a lead potent cytotoxin displaying greater toxicity for neoplasms than normal cells and possesses pleiotropic and suitable druglike properties.

In vitro antitumor activity of *N*-glycosyl sulfonamides

pp 6469–6471

Rosana Crespo, Margarita G. de Bravo, Pedro A. Colinas*, Rodolfo D. Bravo

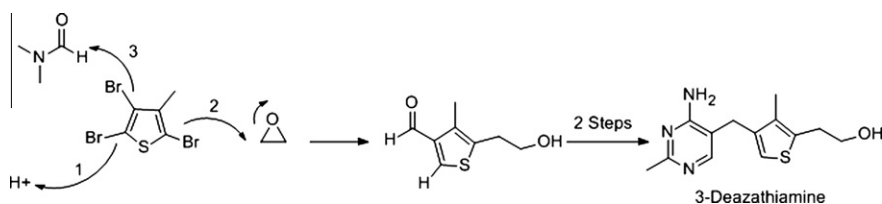


A series of α -D-hex-2-enopyranosyl sulfonamides was evaluated for their antiproliferative activity against human hepatocellular liver carcinoma (HepG2) and human lung adenocarcinoma (A549) cell lines.

A protecting group-free synthesis of deazathiamine: A step toward inhibitor design

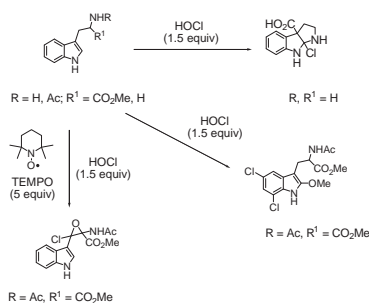
pp 6472–6474

Hong Zhao, Luiz Pedro S. de Carvalho, Carl Nathan, Ouathék Ouerfelli*

**A new insight on the hypochlorous acid scavenging mechanism of tryptamine and tryptophan derivatives**

pp 6475–6478

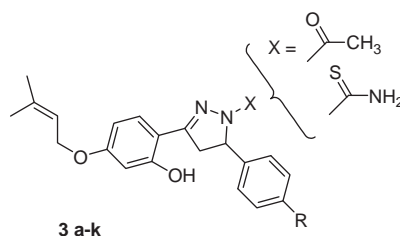
Luísa C. Carvalho, Mónica S. Estevão, Luísa M. Ferreira, Eduarda Fernandes*, M. Manuel B. Marques*



Synthesis and molecular modelling studies of prenylated pyrazolines as MAO-B inhibitors

pp 6479–6482

Rossella Fioravanti*, Adriana Bolasco, Fedele Manna, Francesca Rossi, Francisco Orallo, Matilde Yáñez, Alberto Vitali, Francesco Ortuso, Stefano Alcaro



New prenylated pyrazolines were synthesized and tested on human monoamine oxidase-A and -B isoforms.

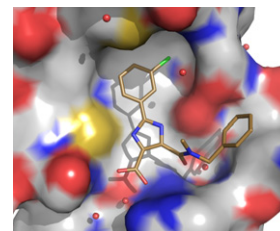
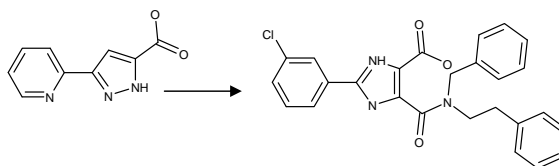


Discovery of cell-active phenyl-imidazole Pin1 inhibitors by structure-guided fragment evolution

pp 6483–6488

Andrew Potter, Victoria Oldfield, Claire Nunns, Christophe Fromont, Stuart Ray, Christopher J. Northfield, Christopher J. Bryant, Simon F. Scrace, David Robinson, Natalia Matossova, Lisa Baker, Pawel Dokurno, Allan E. Surgenor, Ben Davis, Christine M. Richardson, James B. Murray, Jonathan D. Moore*

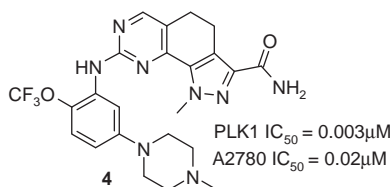
Structure-guided techniques were used to evolve a 5-pyridinyl pyrazole-3-carboxylate fragment into a series of 5-aryl-carbamoyl-3-phenyl-imidazole-4-carboxylates, examples of which inhibited the Pin1 PPIase with sub- μ M IC_{50} and blocked proliferation of prostate cancer cells.



4,5-Dihydro-1H-pyrazolo[4,3-h]quinazolines as potent and selective Polo-like kinase 1 (PLK1) inhibitors

pp 6489–6494

Italo Beria*, Barbara Valsasina, Maria Gabriella Brasca, Walter Ceccarelli, Maristella Colombo, Sabrina Cribioli, Gabriele Fachin, Ronald D. Ferguson, Francesco Fiorentini, Laura M. Gianellini, Maria L. Giorgini, Jurgen K. Moll, Helena Posterl, Daniele Pezzetta, Fulvia Roletto, Francesco Sola, Dania Tesei, Michele Caruso



A 4,5-dihydro-1H-pyrazolo[4,3-h]quinazoline series of Polo-like kinase inhibitors is reported and the SAR disclosed. The series led to low nanomolar PLK1 inhibitors. Compound **4** was tested in vivo showing good antitumor efficacy after iv administration.

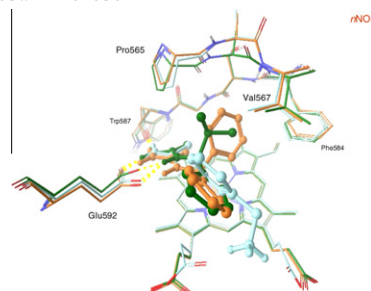


N-Substituted acetamidines and 2-methylimidazole derivatives as selective inhibitors of neuronal nitric oxide synthase

pp 6495–6499

Cristina Maccallini, Antonia Patruno, Fabio Lannutti, Alessandra Ammazalorso, Barbara De Filippis, Marialuigia Fantacuzzi, Sara Franceschelli, Letizia Giampietro, Simona Masella, Mario Felaco, Nazzareno Re*, Rosa Amoroso*

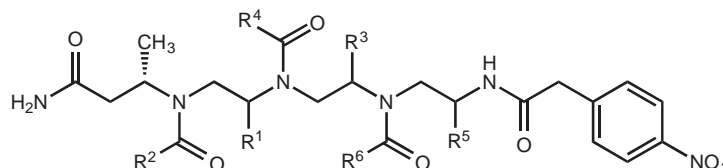
A series of N-substituted acetamidines and 2-methylimidazole derivatives structurally related to W1400 were synthesized and evaluated as Nitric Oxide Synthase (NOS) inhibitors. A molecular modeling study allowed to shed light on the effects of the structural modifications on the selectivity of the designed inhibitors toward the different NOS isoforms.



Solid-phase synthesis and screening of N-acylated polyamine (NAPA) combinatorial libraries for protein binding

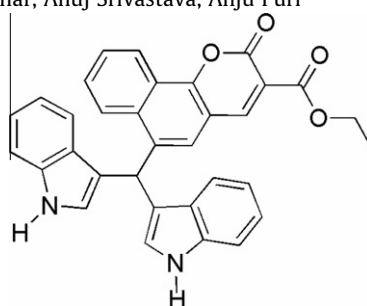
pp 6500–6503

Jaclyn A. Iera, Lisa M. Miller Jenkins, Hiroshi Kajiyama, Jeffrey B. Kopp, Daniel H. Appella*

**Synthesis and antihyperlipidemic activity of novel coumarin bisindole derivatives**

pp 6504–6507

Koneni V. Sashidhara*, Abdhesh Kumar, Manoj Kumar, Anuj Srivastava, Anju Puri

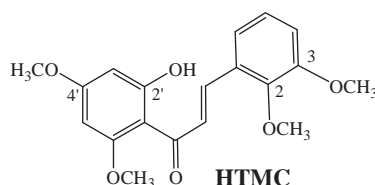


The discovery of new series of coumarin bisindoles as potential antidyslipidemic agents is described.

**Chalcone HTMC causes in vitro selective cytotoxicity, cell-cycle G₁ phase arrest through p53-dependent pathway in human lung adenocarcinoma A549 cells, and in vivo tumor growth suppression**

pp 6508–6512

Yerra Koteswara Rao, Te-Yu Kao, Jiunn-Liang Ko*, Yew-Min Tzeng*



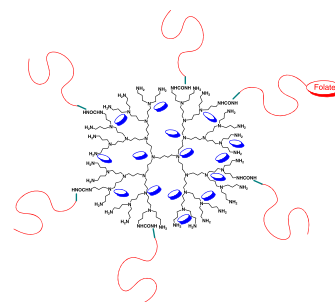
Chalcone derivative 2'-hydroxy-2,3,4',6'-tetramethoxychalcone (HTMC) inhibited the growth of human lung cancer cell lines without cytotoxic to normal cells. In A549 lung adenocarcinoma cells, HTMC caused G₁ phase cell-cycle arrest, inhibited the cell-cycle regulatory proteins phosphorylation of cdc2 (Tyr¹⁵ and Tyr¹⁶¹) and Rb (Ser⁷⁹⁵ and Ser^{807/811}), and accumulated the tumor suppressor genes p53 and p21. In addition, in vivo data demonstrated that HTMC act as a tumor growth suppressing agent.

**Synthesis of a folate functionalized PEGylated poly(propylene imine) dendrimer as prospective targeted drug delivery system**

pp 6513–6517

Zili Sideratou*, Christina Kontoyianni, Garyfalia I. Drossopoulou, Constantinos M. Paleos

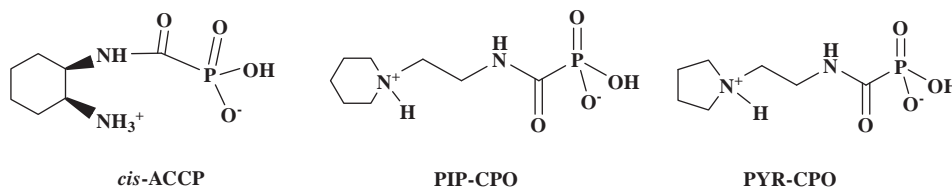
A multifunctional diaminobutane poly(propylene imine) dendrimer bearing a protective PEG-coating and a folate targeting ligand is prepared, which efficiently encapsulates anticancer drug etoposide. This polymer, due to its low toxicity and cell specificity, can be applied as a targeted drug delivery system.



Aminoalkylcarbamoylphosphonates reduce TNF α release from activated immune cells

pp 6518–6523

Efrat Harel, Abraham Rubinstein, Weibin Chen, Eli Breuer*, Boaz Tirosh*

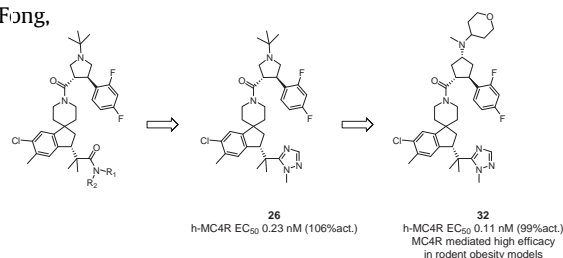


Discovery of highly potent and efficacious MC4R agonists with spiroindane *N*-Me-1,2,4-triazole privileged structures for the treatment of obesity

pp 6524–6532

Shuwen He*, Zhixiong Ye, Peter H. Dobbelaar, Raman K. Bakshi, Qingmei Hong, James P. Dellureficio, Iyassu K. Sebhata, Liangqin Guo, Jian Liu, Tianying Jian, Yingjie Lai, Christopher L. Franklin, Mikhail Reibarkh, Mark A. Holmes, David H. Weinberg, Tanya MacNeil, Rui Tang, Constantin Tamvakopoulos, Qianping Peng, Randy R. Miller, Ralph A. Stearns, Howard Y. Chen, Airu S. Chen, Alison M. Strack, Tung M. Fong, Matthew J. Wyvratt Jr., Ravi P. Nargund

We report an SAR study of MC4R analogs containing spiroindane heterocyclic privileged structures. Compound **26** with *N*-Me-1,2,4-triazole moiety possesses exceptional potency at MC4R and potent anti-obesity efficacy in a mouse model. However, the efficacy is not completely mediated through MC4R. Additional SAR studies led to the discovery of compound **32**, which is more potent at MC4R. Compound **32** demonstrates MC4R mediated anti-obesity efficacy in rodent models.

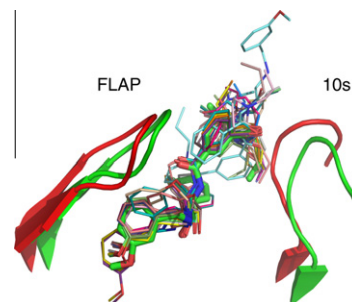


Superimposing the 27 crystal protein/inhibitor complexes of β -secretase to calculate the binding affinities by the linear interaction energy method

pp 6533–6537

Shu Liu, Li-Hua Zhou, Hua-Qiao Wang, Zhi-Bin Yao*

An improved linear interaction energy (LIE) model has been developed to calculate the binding free energies of β -secretase (BACE-1), a diverse set of 27 co-crystallized ligands were put into the binding pocket by superimposing the 27 crystal BACE-1/inhibitor complexes.

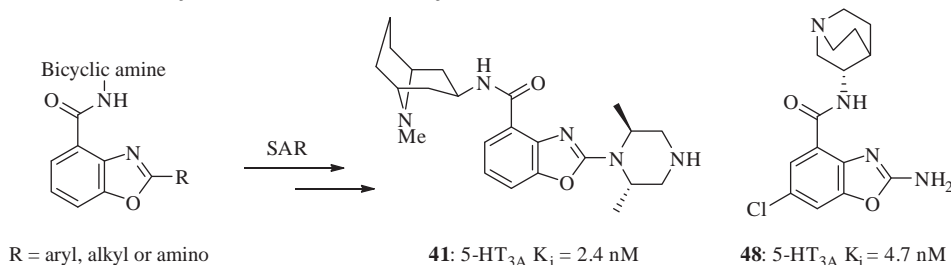


Discovery of 2-substituted benzoxazole carboxamides as 5-HT₃ receptor antagonists

pp 6538–6541

Zhicai Yang, David J. Fairfax, Jun-Ho Maeng, Liaqat Masih, Alexander Usyatinsky, Carla Hassler, Soshanna Isaacson, Kevin Fitzpatrick, Russell J. DeOrazio, Jianqing Chen, James P. Harding, Matthew Isherwood, Svetlana Dobritsa, Kevin L. Christensen, Jonathan D. Wierschke, Brian I. Bliss, Lisa H. Peterson, Cathy M. Beer, Christopher Cioffi, Michael Lynch, W. Martin Rennells, Justin J. Richards, Timothy Rust, Yuri L. Khmel'nitsky, Marlene L. Cohen, David D. Manning*

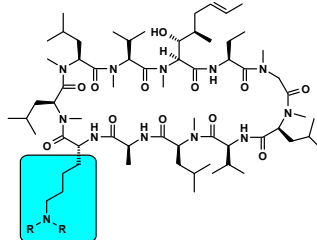
The discovery of a novel series of benzoxazole-4-carboxamides is described. A structure–activity relationship study resulted in the identification of 2-amino benzoxazoles **41** and **48** as selective, orally bioavailable 5-HT₃ receptor antagonists.



Synthesis and biological evaluation of [D-lysine]⁸cyclosporin A analogs as potential anti-HCV agents

pp 6542–6546

Andrew Scribner*, David Houck, Zhuhui Huang, Sarah Mosier, Michael Peel, Bernard Scorneaux



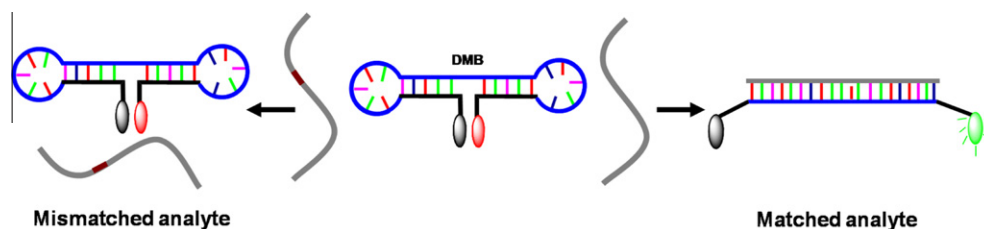
39 R = Me
43 R = Et

An efficient synthesis of [D-lysine]⁸cyclosporin A has been developed. Several analogs of [D-lysine]⁸cyclosporin A have been synthesized and show promising anti-HCV activity, particularly compounds **39** and **43**, which each exhibit an anti-HCV EC₅₀ <200 nM, and are each ≥50-fold less immunosuppressive than cyclosporin A.

A dumbbell molecular beacon for the specific recognition of nucleic acids

pp 6547–6550

Cong Lv, LiLi Yu, Jie Wang, XinJing Tang*

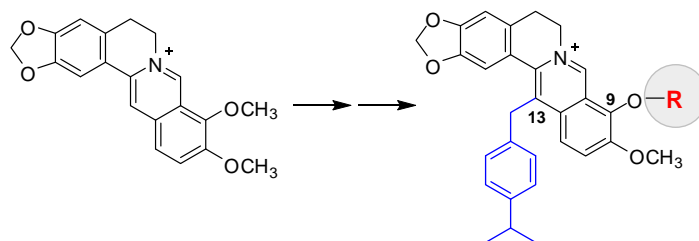


A fluorescent probe with a dumbbell structure for the specific detection of target analyte and mismatched ones.

**Synthesis and antifungal activity of a novel series of 13-(4-isopropylbenzyl)berberine derivatives**

pp 6551–6554

Ki Duk Park, Sung Jin Cho, Jae Sun Moon, Sung Uk Kim*

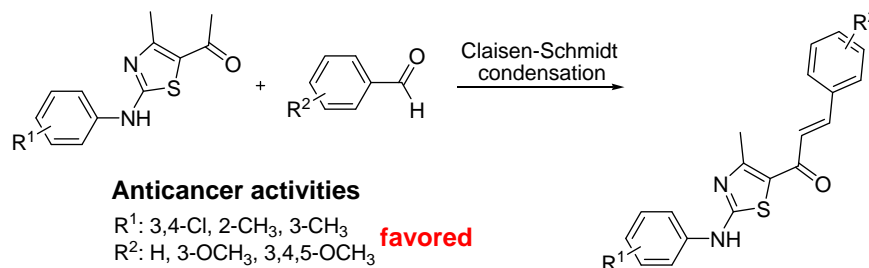


A novel series of 9-O-substituted-13-(4-isopropylbenzyl)berberine derivatives as antifungal agents was synthesized and examined the activity.

**Synthesis and anticancer evaluation of thiazolyl-chalcones**

pp 6555–6559

Hai-Bo Shi, Shi-Jie Zhang, Qiu-Fu Ge, Dian-Wu Guo, Chao-Ming Cai, Wei-Xiao Hu*



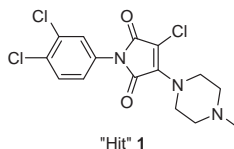
Thiazolyl-chalcones were synthesized via Claisen-Schmidt condensation and their in vitro and in vivo anticancer activities were evaluated.



Inhibition of Bfl-1 with *N*-aryl maleimides

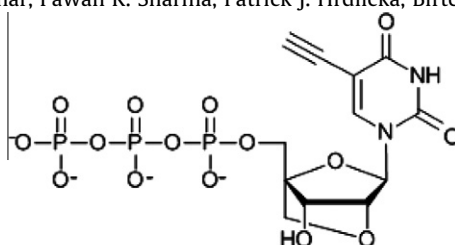
pp 6560–6564

John R. Cashman*, Mary MacDonald, Senait Ghirmai, Karl J. Okolotowicz, Eduard Sergienko, Brock Brown, Xochella Garcia, Dayong Zhai, Russell Dahl, John C. Reed

**Polymerase-directed synthesis of C5-ethynyl locked nucleic acids**

pp 6565–6568

Rakesh N. Veedu*, Harsha V. Burri, Pawan Kumar, Pawan K. Sharma, Patrick J. Hrdlicka, Birte Vester, Jesper Wengel

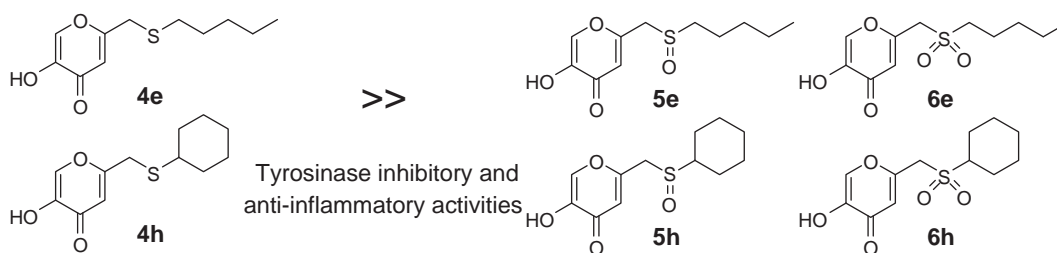
**C5-ethynyl LNA-UTP**

C5-Ethynyl LNA-U nucleoside 5'-triphosphate has been synthesized and investigated the enzymatic recognition capabilities. Phusion and KOD DNA polymerases were found to be efficient to incorporate C5-ethynyl LNA-U nucleotides and afforded full-length extension products.

**Kojyl thioether derivatives having both tyrosinase inhibitory and anti-inflammatory properties**

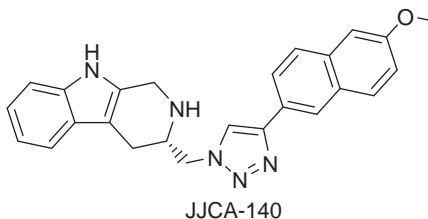
pp 6569–6571

Ho Sik Rho*, Soo Mi Ahn, Dae Sung Yoo, Myung Kyoo Kim, Dong Ha Cho, Jae Youl Cho*

**Triazolyl tryptoline derivatives as β -secretase inhibitors**

pp 6572–6576

Jutamas Jiaranaikulwanitch, Chantana Boonyarat, Valery V. Fokin, Opa Vajragupta*

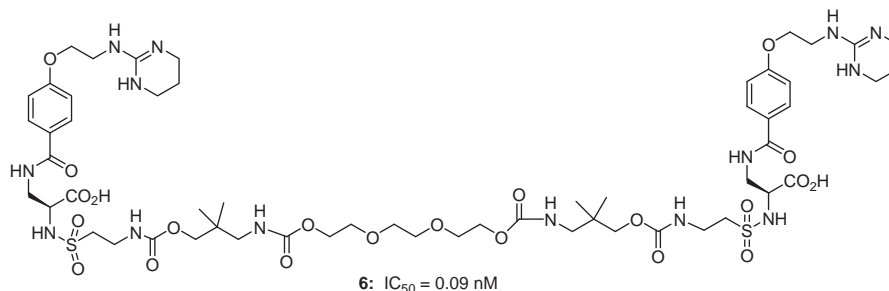


A focused library from 22 different alkynes and an azide-containing tryptoline pharmacophore from virtual screening were synthesized by Cu(I)-catalyzed [3+2] azide-alkyne cycloaddition reaction. The lead compound (JJCA-140) showed IC_{50} of 1.49 μ M against BACE1 and 100 times more selective to BACE1 than Cathepsin-D.



Synthesis and evaluation of bivalent, peptidomimetic antagonists of the $\alpha_v\beta_3$ integrins

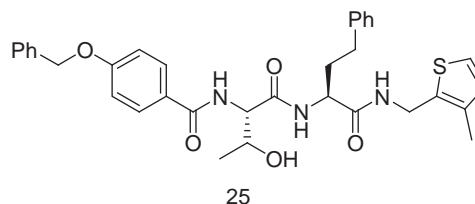
Feng Li, Gouri S. Jas, Guoting Qin, King Li*, Zheng Li*



Optimization of a series of dipeptides with a P3 threonine residue as non-covalent inhibitors of the chymotrypsin-like activity of the human 20S proteasome

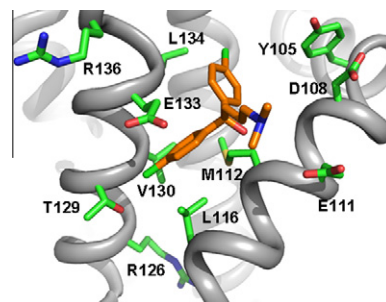
Christopher Blackburn*, Cynthia Barrett, Jonathan L. Blank, Frank J. Bruzzese, Nancy Bump, Lawrence R. Dick, Paul Fleming, Khristofer Garcia, Paul Hales, Zhigen Hu, Matthew Jones, Jane X. Liu, Darshan S. Sappal, Michael D. Sintchak, Christopher Tsu, Kenneth M. Gigstad

Starting from a tripeptide screening hit, a series of dipeptide inhibitors of the proteasome with Thr as the P3 residue has been optimized with the aid of crystal structures in complex with the β -5/6 active site of γ 20S. Derivative **25**, (β 5 IC_{50} = 7.4 nM) inhibits only the chymotryptic activity of the proteasome, shows cellular activity against targets in the UPS, and inhibits proliferation.



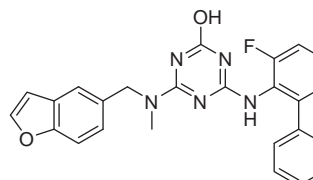
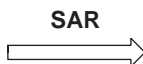
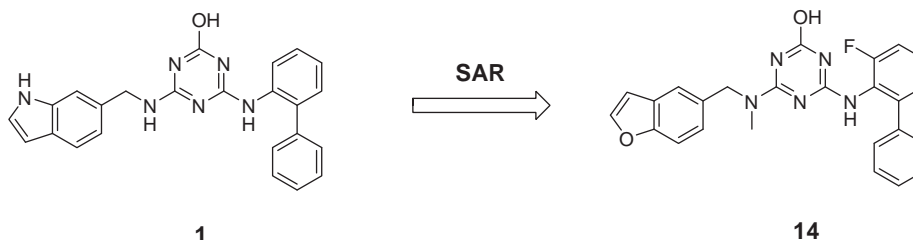
Discovery of a potent and selective Bcl-2 inhibitor using SAR by NMR

Andrew M. Petros, Jeffrey R. Huth, Thorsten Oost, Cheol-Min Park, Hong Ding, Xilu Wang, Haichao Zhang, Paul Nimmer, Renaldo Mendoza, Chaohong Sun, Jamey Mack, Karl Walter, Sarah Dorwin, Emily Gramling, Uri Lador, Saul H. Rosenberg, Steven W. Elmore, Stephen W. Fesik, Philip J. Hajduk*



Discovery and SAR of a series of 4,6-diamino-1,3,5-triazin-2-ol as novel non-nucleoside reverse transcriptase inhibitors of HIV-1

Bin Liu*, Younghee Lee, Jinming Zou, H. Michael Petrassi, Rhoda W. Joseph, Wenchun Chao, Enrique L. Michelotti, Marina Bukhtiyarova, Eric B. Springman, Bruce D. Dorsey

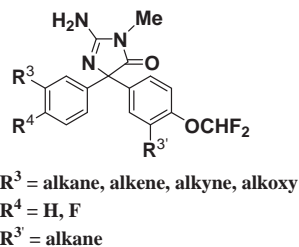


Discovery and SAR of a series of 4,6-diamino-1,3,5-triazin-2-ol as novel non-nucleoside reverse transcriptase inhibitors (NNRTIs) of HIV-1 is described.

Design and synthesis of aminohydantoin s as potent and selective human β -secretase (BACE1) inhibitors with enhanced brain permeability

pp 6597–6605

Michael S. Malamas*, Albert Robichaud, Jim Erdei, Dominick Quagliato, William Solvibile, Ping Zhou, Koi Morris, Jim Turner, Erik Wagner, Kristi Fan, Andrea Olland, Steve Jacobsen, Peter Reinhart, David Riddell, Menelas Pangalos

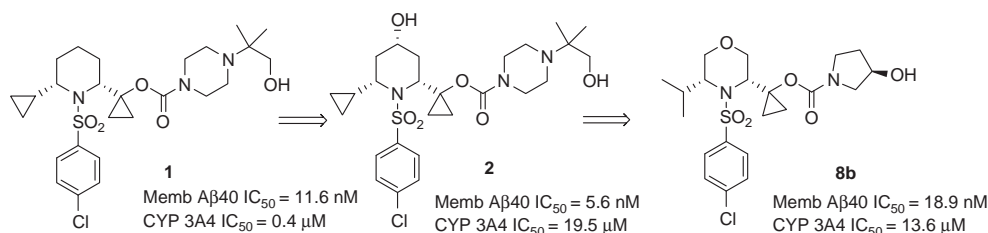


Small R^3 groups decrease P-gP affinity, TPSA, and molecular weight, which result in enhancement of the brain permeability of the compound.

Design, synthesis, and structure–activity relationship studies of *N*-arylsulfonyl morpholines as γ -secretase inhibitors

pp 6606–6609

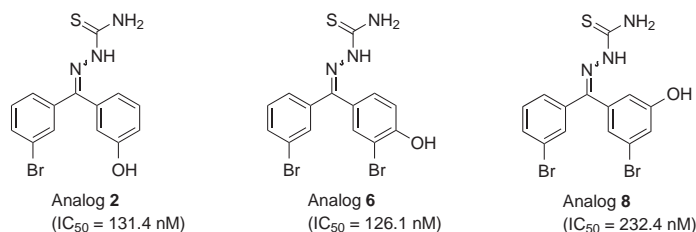
Hongmei Li*, Ruo Xu*, David Cole, John W. Clader, William J. Greenlee, Amin A. Nomeir, Lixin Song, Lili Zhang



Functionalized benzophenone, thiophene, pyridine, and fluorene thiosemicarbazone derivatives as inhibitors of cathepsin L

pp 6610–6615

G. D. Kishore Kumar, Gustavo E. Chavarria, Amanda K. Charlton-Sevcik, Grace Kim Yoo, Jiangli Song, Tracy E. Strecker, Bronwyn G. Siim, David J. Chaplin, Mary Lynn Trawick, Kevin G. Pinney*



Brominated-benzophenone thiosemicarbazone inhibitors of cathepsin L.

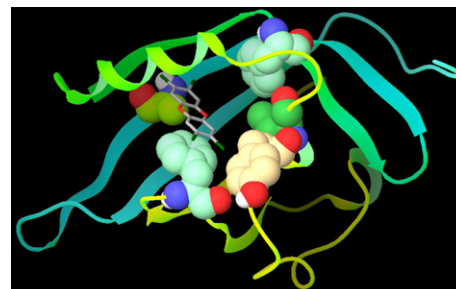


Identification of optimum computational protocols for modeling the aryl hydrocarbon receptor (AHR) and its interaction with ligands

pp 6616–6619

Ashutosh S. Jogalekar*, Stephan Reiling, Roy J. Vaz

The aryl hydrocarbon receptor (AHR) is one of the principal xenobiotic receptors in living organisms and is responsible for interacting with several drugs and environmental toxins, most notably tetrachlorodiben-zodioxin (TCDD). Binding of diverse agonists to AHR initiates an extensive set of downstream gene expression responses and thus identifies AHR among a key set of proteins responsible for mediating interactions between living organisms and foreign molecules. While extensive biochemical investigations on the interaction of AHR with ligands have been carried out, studies comparing the abilities of specific computational algorithms in explaining the potency of known AHR ligands are lacking. In this study we use molecular dynamics simulations to identify a physically realistic conformation of the AHR that is relevant to ligand binding. We then use two sets of existing data on known AHR ligands to evaluate the performance of several docking and scoring protocols in rationalizing the potencies of these ligands. The results identify an optimum set of protocols that could prove useful in future AHR ligand discovery and design as a target or anti-target. Exploration of the details of these protocols sheds light on factors operating in modeling AHR ligand binding.

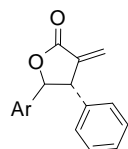


Tailored α -methylene- γ -butyrolactones and their effects on growth suppression in pancreatic carcinoma cells

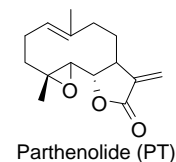
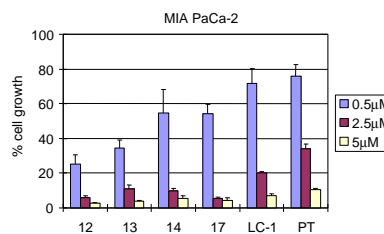
pp 6620–6623

P. Veeraraghavan Ramachandran*, Debarshi Pratihari, Hari Narayanan G. Nair, Matthew Walters, Sadie Smith, Michele T. Yip-Schneider, Huangbing Wu, C. Max Schmidt

A selected series of α -methylene- γ -butyrolactones (AMGBL) were synthesized via allylboration and a discernible relationship between the substitution pattern and anti-proliferative activity was established by screening against three human pancreatic cancer cell lines; β,γ -diaryl-AMGBLs exhibited higher potency than parthenolide and LC-1.

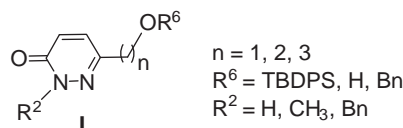


Ar = Ph: **12**
 Ar = 4-MeOPh: **13**
 Ar = 4-MePh: **14**
 Ar = 2-Naphthyl: **17**

**New pyridazinone derivatives with vasorelaxant and platelet antiaggregatory activities**

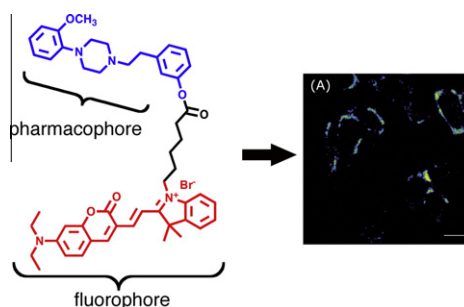
pp 6624–6627

Tamara Costas, Pedro Besada, Alessandro Piras, Laura Acevedo, Matilde Yañez, Francisco Orallo, Reyes Laguna, Carmen Terán*

**Identification of a red-emitting fluorescent ligand for in vitro visualization of human serotonin 5-HT_{1A} receptors**

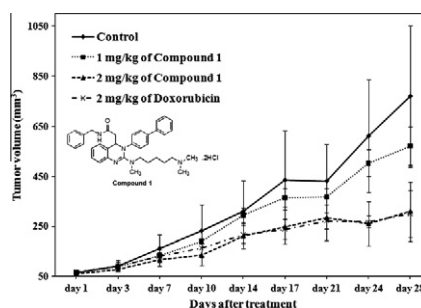
pp 6628–6632

Enza Lacivita, Anna Carmela Masotti, Md. Jafurulla, Roopali Saxena, Nandini Rangaraj, Amitabha Chattopadhyay, Nicola A. Colabufo, Francesco Berardi, Roberto Perrone, Marcello Leopoldo*

**Antitumor activity of 3,4-dihydroquinazoline dihydrochloride in A549 xenograft nude mice**

pp 6633–6636

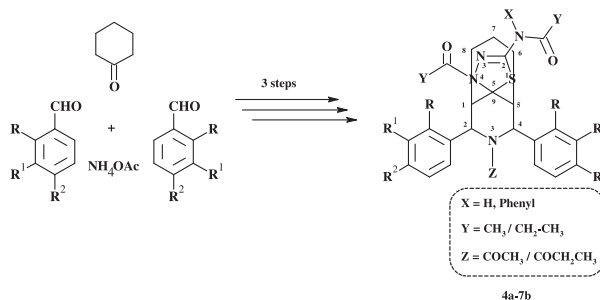
Soo Yeon Jung, So Hyung Lee, Han Byul Kang, Hang Ah Park, Sun Ki Chang, Jungahn Kim, Dong Joon Choo, Chun Rim Oh, Young Deuk Kim, Ji Hyung Seo, Kyung-Tae Lee, Jae Yeol Lee*



Efficient synthesis, spectral analysis and antimicrobial studies of nitrogen and sulfur containing spiro heterocycles from 2,4-diaryl-3-azabicyclo[3.3.1]nonan-9-ones

pp 6637–6643

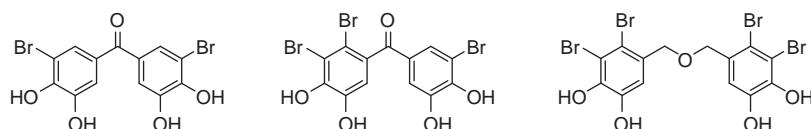
M. Rani, R. Ramachandran, S. Kabilan*



Bromophenols as *Candida albicans* isocitrate lyase inhibitors

pp 6644–6648

Ki-Bong Oh, Heung Bae Jeon, Yu-Ri Han, Yeon-Ju Lee, Jiyoung Park, So-Hyoung Lee, Dongsik Yang, Mihyun Kwon, Jongheon Shin, Hyi-Seung Lee*

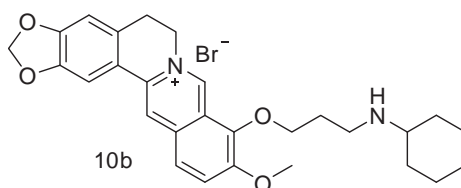


The synthesis and bioactivity of bromophenols are described.

Berberine derivatives, with substituted amino groups linked at the 9-position, as inhibitors of acetylcholinesterase/butyrylcholinesterase

pp 6649–6652

Ling Huang, Zonghua Luo, Feng He, Anding Shi, Fangfei Qin, Xingshu Li*



Berberine derivatives with substituted amino groups linked on the 9-position of berberine with different carbon spacers were designed, synthesized, and biologically evaluated as inhibitors of acetylcholinesterase. Compound **10b** with a cyclohexylamino group linked to berberine by a three carbon spacer, gave the most potent inhibitor activity with an IC₅₀ value of 0.020 μM for AchE.

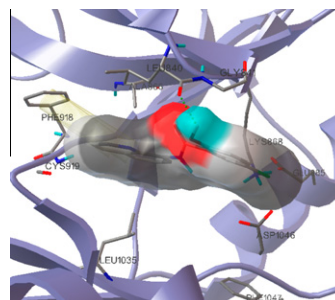


Design, synthesis and biological evaluation of quinoline amide derivatives as novel VEGFR-2 inhibitors

pp 6653–6656

Ying Yang, Lei Shi, Yang Zhou, Huan-Qiu Li, Zhen-Wei Zhu, Hai-Liang Zhu*

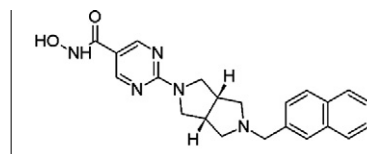
Two series of quinoline amide derivatives were prepared and found to be good inhibitors of vascular endothelial growth factor receptor-2 (VEGFR-2). The inhibitory activities were investigated against VEGFR-2 kinase and human umbilical vein endothelial cells (HUVEC) in vitro. Compound **6** (5-chloro-2-hydroxy-N-(quinolin-8-yl)benzamide) exhibited the most potent inhibitory activity (IC₅₀ = 3.8 and 5.5 nM for VEGFR-2 kinase and HUVEC, respectively). Docking simulation was performed to position compound **6** into the VEGFR-2 ATP-binding site to determine the probable binding model. The results supported the initial pharmacophoric hypothesis and suggested a common mode of interaction at the ATP-binding site of VEGFR-2.



Design and synthesis of novel pyrimidine hydroxamic acid inhibitors of histone deacetylases

pp 6657–6660

Alastair D. G. Donald*, Vanessa L. Clark, Sanjay Patel, Francesca A. Day, Martin G. Rowlands, Judata Wibata, Lindsay Stimson, Anthea Hardcastle, Sue A. Eccles, Deborah McNamara, Lindsey A. Needham, Florence I. Raynaud, Wynne Aherne, David F. Moffat

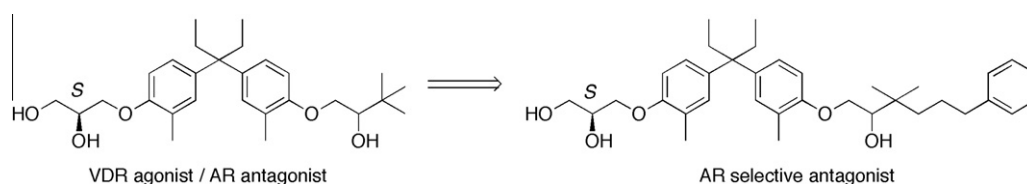


Compound **13** HDAC IC₅₀ 13 nM
 HCT-116 120 nM
 HeLa 260 nM
 Orally active in HCT-116 xenograft model

**Novel selective anti-androgens with a diphenylpentane skeleton**

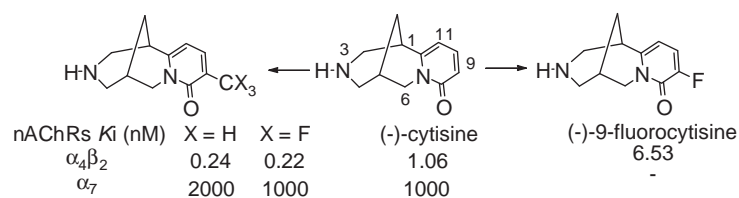
pp 6661–6666

Keisuke Maruyama, Tomomi Noguchi-Yachide, Kazuyuki Sugita, Yuichi Hashimoto, Minoru Ishikawa*

**Identification of 9-fluoro substituted (–)-cytisine derivatives as ligands with high affinity for nicotinic receptors**

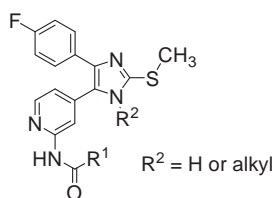
pp 6667–6670

Nicolas Houllier, JaganMohan Gopiseti, Pierre Lestage, Marie-Claire Lasne, Jacques Rouden*

**Tri- and tetrasubstituted imidazoles as p38α mitogen-activated protein kinase inhibitors**

pp 6671–6675

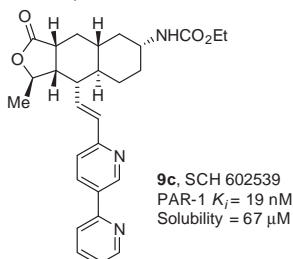
Stefan Laufer*, Dominik Hauser, Thomas Stegmüller, Claudia Bracht, Kathrin Ruff, Verena Schattel, Wolfgang Albrecht, Pierre Koch



Discovery of a vorapaxar analog with increased aqueous solubility

pp 6676–6679

Yan Xia*, Samuel Chackalamannil, William J. Greenlee, Yuguang Wang, Zhiyong Hu, Yuriko Root, Jesse Wong, Jianshe Kong, Ho-Sam Ahn, George Boykow, Yunsheng Hsieh, Stan Kurowski, Madhu Chintala

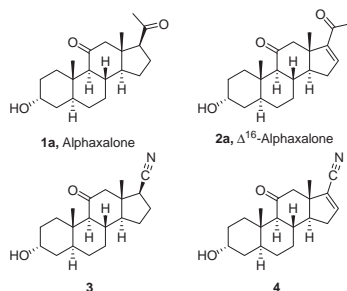


An analog of the thrombin receptor antagonist vorapaxar (SCH 530348) with increased aqueous solubility, compound **9c** (SCH 602539), was discovered through incorporation of polar substituents on the pyridine ring of the himbacine-derived lead series.

Neurosteroid analogues. 15. A comparative study of the anesthetic and GABAergic actions of alphaxalone, Δ^{16} -alphaxalone and their corresponding 17-carbonitrile analogues

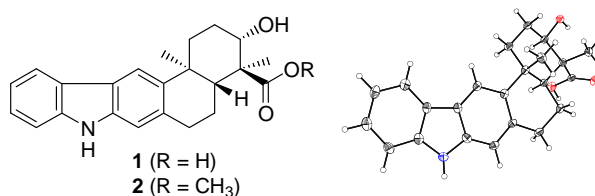
pp 6680–6684

Achintya K. Bandyopadhyaya, Brad D. Manion, Ann Benz, Amanda Taylor, Nigam P. Rath, Alex S. Evers, Charles F. Zorumski, Steven Mennerick, Douglas F. Covey*

**Xiamycin, a pentacyclic indolosesquiterpene with selective anti-HIV activity from a bacterial mangrove endophyte**

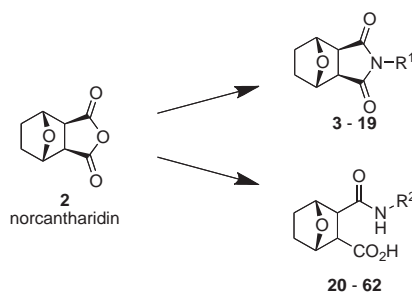
pp 6685–6687

Ling Ding, Jan Münch, Helmar Goerls, Armin Maier, Heinz-Herbert Fiebig, Wen-Han Lin, Christian Hertweck*

**The antiplasmodial activity of norcantharidin analogs**

pp 6688–6695

Joanna Bajsa*, Adam McCluskey, Christopher P. Gordon, Scott G. Stewart, Timothy A. Hill, Rajnish Sahu, Stephen O. Duke, Babu L. Tekwani

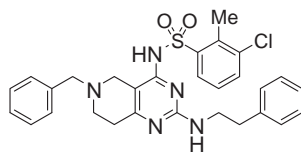


The antiplasmodial activity of 60 norcantharidin analogs is reported.

5,6,7,8-Tetrahydropyrido[4,3-d]pyrimidines as novel class of potent and highly selective CaMKII inhibitors

pp 6696–6698

Shigehiro Asano*, Masafumi Komiya, Nobuyuki Koike, Erina Koga, Shogo Nakatani, Yoshiaki Isobe

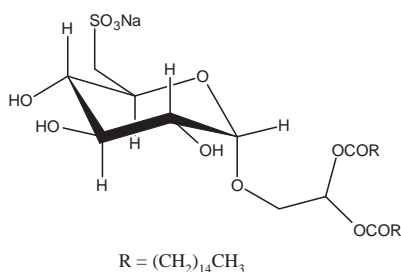


8p
CaMKII Inhibition; $IC_{50} = 0.063 \mu M$

**Identification of a sulfonoquinovosyldiacylglyceride from *Azadirachta indica* and studies on its cytotoxic activity and DNA binding properties**

pp 6699–6702

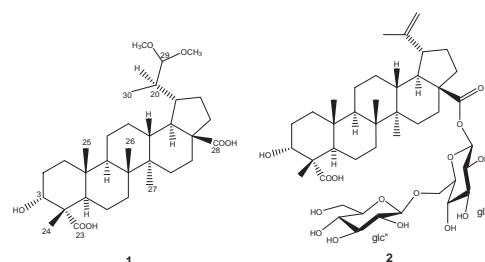
Ratna Chatterjee, Omkar Singh, Lalawmpuii Pachuau, Shiba Prasad Malik, Mausumi Paul, Kakali Bhadra, Santanu Paul, Gopinatha Suresh Kumar, Nirup Bikash Mondal, Sukdeb Banerjee*

**Lupane-type triterpenoids from the steamed leaves of *Acanthopanax koreanum* and their inhibitory effects on the LPS-stimulated pro-inflammatory cytokine production in bone marrow-derived dendritic cells**

pp 6703–6707

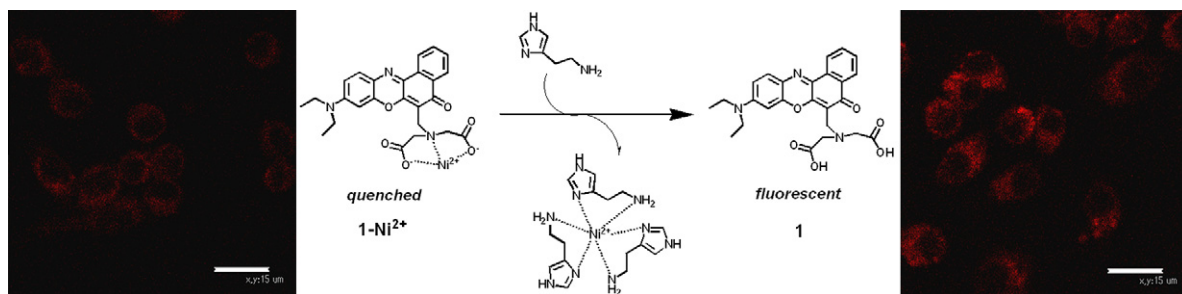
Jeong Ah Kim, Seo Young Yang, Jung-Eun Koo, Young-Sang Koh, Young Ho Kim*

Phytochemical investigation resulted in isolation of two new lupane-type triterpenoids (**1** and **2**) from the steamed leaves of *Acanthopanax koreanum* (Araliaceae). Compound **1** significantly inhibited LPS-stimulated IL-12, IL-6, and TNF- α production in bone marrow-derived dendritic cells.

**An amphiphilic fluorescent probe for the visualization of histamine in living cells**

pp 6708–6711

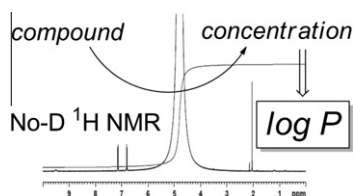
Daisuke Seto, Nobuaki Soh, Koji Nakano, Toshihiko Imato*



A practical deuterium-free NMR method for the rapid determination of 1-octanol/water partition coefficients of pharmaceutical agents

pp 6712–6715

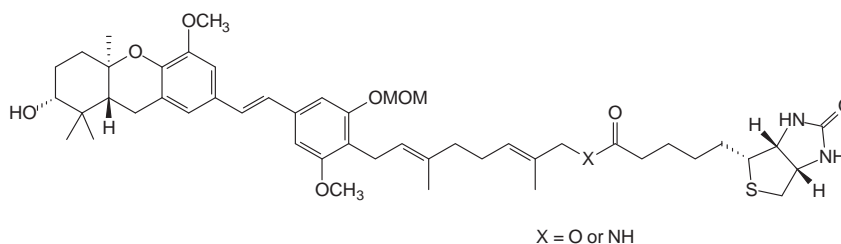
Huaping Mo*, Kathryn M. Balko, David A. Colby*



Biologically active biotin derivatives of schweinfurthin F

pp 6716–6720

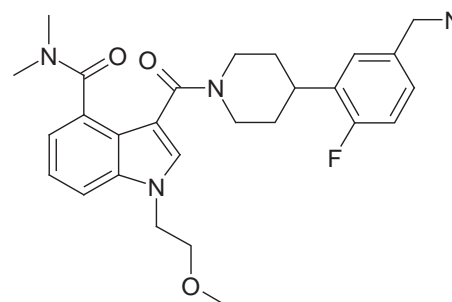
Natalie C. Ulrich, Craig H. Kuder, Raymond J. Hohl, David F. Wiemer*



A conformationally constrained inhibitor with an enhanced potency for β -tryptase and stability against semicarbazide-sensitive amine oxidase (SSAO)

pp 6721–6724

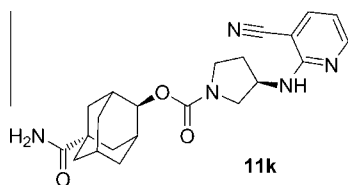
Guyan Liang*, Yong Mi Choi-Sledeski, Gregory Poli, Xin Chen, Patrick Shum, Anne Minnich, Qingping Wang, Joseph Tsay, Keith Sides, Jennifer Cairns, Gregory Stoklosa, Thaddeus Nieduzak, Zhicheng Zhao, Jie Wang, Roy J. Vaz

Conformationally constrained β -tryptase inhibitor.

Discovery and optimization of adamantyl carbamate inhibitors of 11 β -HSD1

pp 6725–6729

Colin M. Tice*, Wei Zhao, Paula M. Krosky, Barbara A. Kruk, Jennifer Berbaum, Judith A. Johnson, Yuri Bukhtiyarov, Reshma Panemangalore, Boyd B. Scott, Yi Zhao, Joseph G. Bruno, Lamont Howard, Jennifer Togias, Yuan-Jie Ye, Suresh B. Singh, Brian M. McKeever, Peter R. Lindblom, Joan Guo, Rong Guo, Herbert Nar, Annette Schuler-Metz, Richard E. Gregg, Katerina Leftheris, Richard K. Harrison, Gerard M. McGeehan, Linghang Zhuang, David A. Claremon

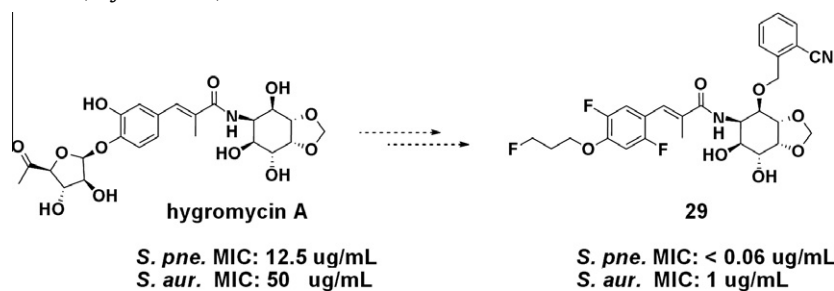
Human 11 β -HSD1 enzyme IC₅₀ = 0.9 nMHuman 11 β -HSD1 adipocyte IC₅₀ = 0.4 nMRat liver microsome t_{1/2} > 60 min

%F (rat) = 42

Synthesis and biological evaluation of novel hygromycin A antibacterial agents

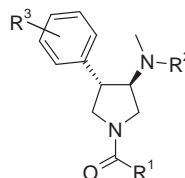
pp 6730–6734

Michael S. Visser, Kevin D. Freeman-Cook*, Steven J. Brickner, Katherine E. Brighty, Phuong T. Le, Sarah K. Wade, Rhonda Monahan, Gary J. Martinelli, Kyle T. Blair, Dianna E. Moore

**Rational design of novel pyrrolidine derivatives as orally active neurokinin-3 receptor antagonists**

pp 6735–6738

Hassen Ratni*, Theresa M. Ballard, Caterina Bissantz, Torsten Hoffmann, Philippe Jablonski, Frederic Knoflach, Henner Knust, Parichehr Malherbe, Matthias Nettekoven, Angelique Patiny-Adam, Claus Riemer, Monique Schmitt, Will Spooren



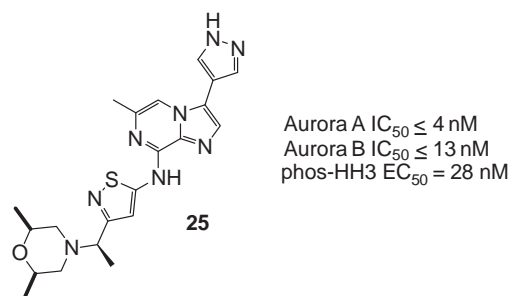
The rational design of a novel series of orally active NK3R antagonists is described.

Discovery of orally bioavailable imidazo[1,2-*a*]pyrazine-based Aurora kinase inhibitors

pp 6739–6743

David B. Belanger*, Michael J. Williams, Patrick J. Curran, Amit K. Mandal, Zhaoyang Meng, Matthew P. Rainka, Tao Yu, Neng-Yang Shih, M. Arshad Siddiqui, Ming Liu, Seema Tevar, Suining Lee, Lianzhu Liang, Kimberly Gray, Bohdan Yaremko, Jennifer Jones, Elizabeth B. Smith, Dan B. Prelusky, Andrea D. Basso

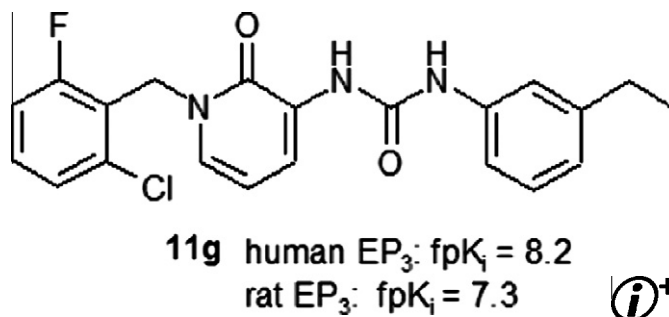
We report a series of potent imidazo[1,2-*a*]pyrazine-based Aurora kinase inhibitors. Optimization of the solvent accessible 8-position led to improvements in both oral bioavailability and off-target kinase inhibition. Compound **25** demonstrates anti-tumor activity in an A2780 ovarian tumor xenograft model.

**3-Urea-1-(phenylmethyl)-pyridones as novel, potent, and selective EP₃ receptor antagonists**

pp 6744–6747

Yue H. Li*, Pei-San Tseng, Karen A. Evans, Jon-Paul Jaworski, Dwight M. Morrow, Harvey E. Fries, Charlene W. Wu, Richard M. Edwards, Jian Jin*

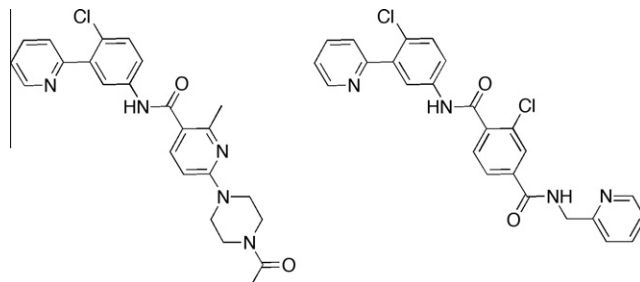
A series of 3-urea-1-(phenylmethyl)-pyridones was discovered as novel EP₃ antagonists via high-throughput screening and subsequent optimization. The synthesis, structure–activity relationships, and optimization of the initial hit that resulted in potent and selective EP₃ receptor antagonists such as **11g** are described.



Second generation 2-pyridyl biphenyl amide inhibitors of the hedgehog pathway

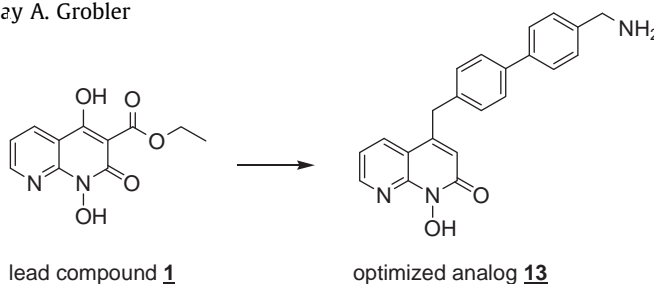
pp 6748–6753

Georgette M. Castanedo, Shumei Wang, Kirk D. Robarge, Elizabeth Blackwood, Daniel Burdick, Christine Chang, Gerrit J. P. Dijkgraaf, Stephen Gould, Janet Gunzner, Oivin Guichert, Jason Halladay, Cyrus Khojasteh, Leslie Lee, James C. Marsters Jr., Lesley Murray, David Peterson, Emile Plise, Laurent Salphati, Frederic J. de Sauvage, Susan Wong, Daniel P. Sutherlin*

**Potent and selective HIV-1 ribonuclease H inhibitors based on a 1-hydroxy-1,8-naphthyridin-2(1H)-one scaffold**

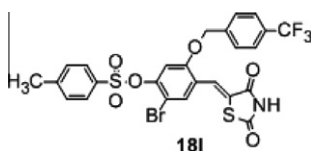
pp 6754–6757

Peter D. Williams*, Donnette D. Staas, Shankar Venkatraman, H. Marie Loughran, Rowena D. Ruzek, Theresa M. Booth, Terry A. Lyle, John S. Wai, Joseph P. Vacca, Bradley P. Feuston, Linda T. Ecto, Jessica A. Flynn, Daniel J. DiStefano, Daria J. Hazuda, Carolyn M. Bahnck, Amy L. Himmelberger, Geetha Dornadula, Renee C. Hrin, Kara A. Stillmock, Marc V. Witmer, Michael D. Miller, Jæy A. Grobler

**Novel thiazolidinedione derivatives with anti-obesity effects: Dual action as PTP1B inhibitors and PPAR- γ activators**

pp 6758–6763

Bharat Raj Bhattarai, Bhooshan Kafle, Ji-Sun Hwang, Seung Wook Ham, Keun-Hyeung Lee, Hwangseo Park, Inn-Oc Han*, Hyeongjin Cho*

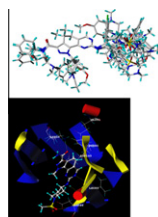


Compound **18I** was a PTP1B inhibitor with IC_{50} of 1.3 μ M and activated PPAR- γ at 1.0 μ M. It suppressed weight gain in a DIO mouse model system.

**3D-QSAR and docking studies on pyrazolo[4,3-*h*]quinazoline-3-carboxamides as cyclin-dependent kinase 2 (CDK2) inhibitors**

pp 6764–6772

Ping Lan, Wan-Na Chen, Gao-Keng Xiao, Ping-Hua Sun*, Wei-Min Chen*

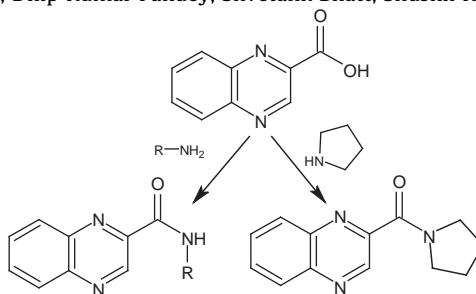


3D-QSAR and docking studies were performed on a series of pyrazolo[4,3-*h*]quinazoline-3-carboxamides as CDK2/CyA inhibitors. The correlation of the results obtained from 3D-QSAR and docking studies can be served as a useful guideline for the further modification of pyrazolo[4,3-*h*]quinazoline-3-carboxamides that function as CDK2/CyA inhibitors.

Design, synthesis and structure–activity relationship of novel quinoxalin-2-carboxamides as 5-HT₃ receptor antagonists for the management of depression

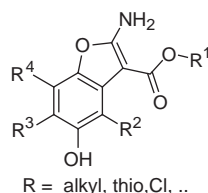
pp 6773–6776

Radhakrishnan Mahesh, Thangaraj Devadoss*, Dilip Kumar Pandey, Shvetank Bhatt, Shushil Kumar Yadav

Synthesis, 5-HT₃ receptor antagonistic and anti-depressant-like activity of novel quinoxalin-2-carboxamides are described.**Synthesis and antifungal activity of benzofuran-5-ols**

pp 6777–6780

Chung-Kyu Ryu*, Ae Li Song, Jung Yoon Lee, Jung An Hong, Joo Hee Yoon, Aram Kim

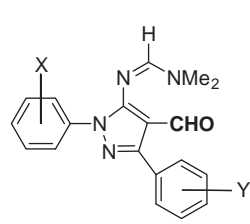


Benzofuran-5-ol derivatives were synthesized and tested for in vitro antifungal activity against pathogenic fungi. Among them tested, many of benzofuran-5-ols exhibited potent antifungal activity.

Synthesis and antiproliferative evaluation of *N,N*-disubstituted-*N'*-[1-aryl-1*H*-pyrazol-5-yl]-methanimidamides

pp 6781–6784

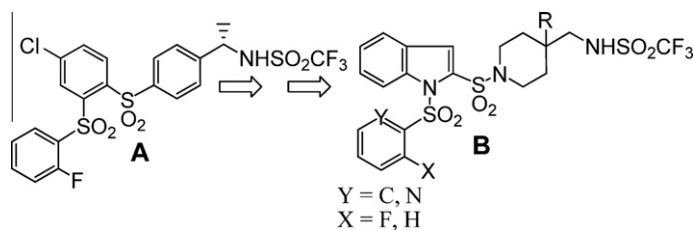
Kaung-Min Cheng, Yu-Ying Huang, Jiann-Jyh Huang, Kimiyoshi Kaneko, Masayuki Kimura, Hiroyuki Takayama, Shin-Hun Juang*, Fung Fuh Wong*

	X	Y	GI ₅₀ (μM) for Antiproliferative activity		
			NCI-H661	NPC-TW01	Jurkat
	<i>m</i> -Cl	H	6.9	6.4	8.3
	<i>p</i> -Br	H	6.7	7.4	7.3
	H	<i>p</i> -Me	11.9	9.7	9.5
	H	<i>p</i> -Cl	8.6	8.1	7.9

**Expansion of SAR studies on triaryl bis sulfone cannabinoid CB₂ receptor ligands**

pp 6785–6789

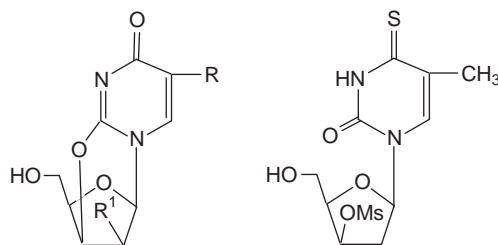
Ling Tong*, B. B. Shankar*, Lei Chen, Razia Rizvi, Joseph Kelly, Eric Gilbert, Chunli Huang, De-Yi Yang, Joseph A. Kozlowski, N.-Y. Shih, W. Gonsiorek, R. William Hipkin, Asra Malikzay, Charles A. Lunn, Daniel J. Lundell

SAR exploration on triaryl bis sulfone **A** led us to structurally novel and diverse CB₂ selective ligands **B**.

Antiviral activity of 2,3'-anhydro and related pyrimidine nucleosides against hepatitis B virus

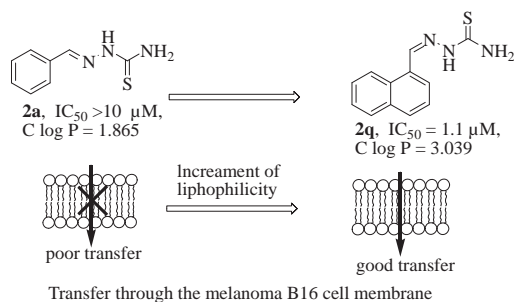
pp 6790–6793

Naveen C. Srivastav, Michelle Mak, Babita Agrawal, D. Lorne J. Tyrrell, Rakesh Kumar*

**Structural characteristics of thiosemicarbazones as inhibitors of melanogenesis**

pp 6794–6796

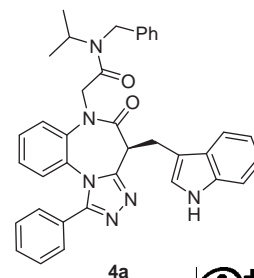
Ki-Cheul Lee, Pillaiyar Thanigaimalai, Vinay K. Sharma, Min-Seok Kim, Eunmri Roh, Bang-Yeon Hwang, Youngsoo Kim, Sang-Hun Jung*

**Discovery of *N*-benzyl-2-[(4*S*)-4-(1*H*-indol-3-ylmethyl)-5-oxo-1-phenyl-4,5-dihydro-6*H*-[1,2,4]triazolo[4,3-*a*]-[1,5]benzodiazepin-6-yl]-*N*-isopropylacetamide, an orally active, gut-selective CCK1 receptor agonist for the potential treatment of obesity**

pp 6797–6801

Richard L. Elliott, Kimberly O. Cameron*, Janice E. Chin, Jeremy A. Bartlett, Elena E. Beretta, Yue Chen, Paul Da Silva Jardine, Jeffrey S. Dubins, Melissa L. Gillaspay, Diane M. Hargrove, Amit S. Kalgutkar, Janet A. LaFlamme, Mary E. Lame, Kelly A. Martin, Tristan S. Maurer, Nancy A. Nardone, Robert M. Oliver, Dennis O. Scott, Dexue Sun, Andrew G. Swick, Catherine E. Trebino, Yingxin Zhang

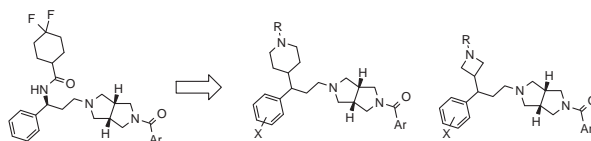
We report the design, synthesis, and SAR of triazolobenzodiazepinone CCK1 receptor agonists. Compound **4a** is a potent, selective CCK1 receptor agonist which reduces food intake in rodents with minimal systemic exposure.

**Evaluation of amide replacements in CCR5 antagonists as a means to increase intrinsic permeability.**

pp 6802–6807

Part 2: SAR optimization and pharmacokinetic profile of a homologous azacycle series

Jutta Wanner*, Lijing Chen, Rémy C. Lemoine, Rama Kondru, Andreas Jekle, Gabrielle Heilek, André deRosier, Changhua Ji, Pamela W. Berry, David M. Rotstein

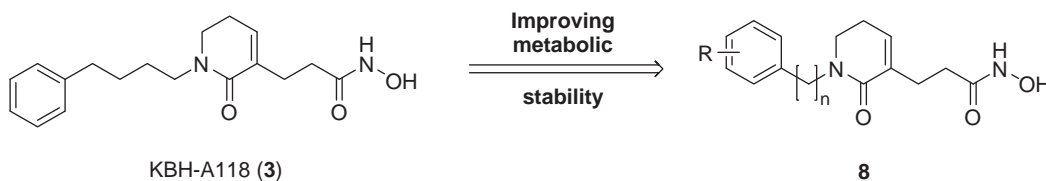


In our CCR5 program, piperidine and azetidine amide replacements as means to improve intrinsic permeability were evaluated. This led to new series of potent CCR5 antagonists, with improved PK behavior.

Property based optimization of δ -lactam HDAC inhibitors for metabolic stability

pp 6808–6811

Hong Chul Yoon, Eunhyun Choi, Jung Eun Park, Misun Cho, Jeong Jea Seo, Soo Jin Oh, Jong Soon Kang, Hwan Mook Kim, Song-Kyu Park, Kiho Lee*, Gyoonee Han*

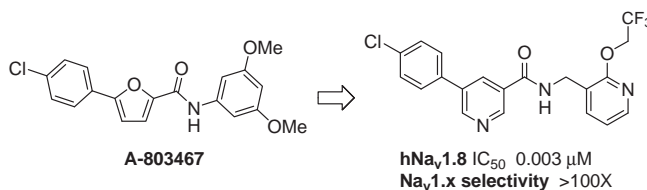


To improve metabolic stability, various analogues were prepared with substituents on aromatic ring of cap group and various chain lengths between the cap group and δ -lactam core.

**Subtype-selective $\text{Na}_v1.8$ sodium channel blockers: Identification of potent, orally active nicotinamide derivatives**

pp 6812–6815

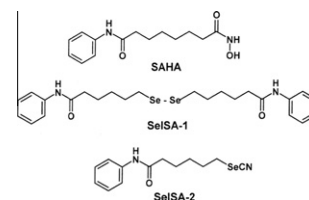
Michael E. Kort*, Robert N. Atkinson, James B. Thomas, Irene Drizin, Matthew S. Johnson, Matthew A. Secrest, Robert J. Gregg, Marc J. C. Scanio, Lei Shi, Ahmed H. Hakeem, Mark A. Matulenko, Mark L. Chapman, Michael J. Krambis, Dong Liu, Char-Chang Shieh, XuFeng Zhang, Gricelda Simler, Joseph P. Mikusa, Chengmin Zhong, Shailen Joshi, Prisca Honore, Rosemarie Roeloffs, Stephen Werness, Brett Antonio, Kennan C. Marsh, Connie R. Faltynek, Douglas S. Krafte, Michael F. Jarvis, Brian E. Marron*

**Selenium-containing analogs of SAHA induce cytotoxicity in lung cancer cells**

pp 6816–6819

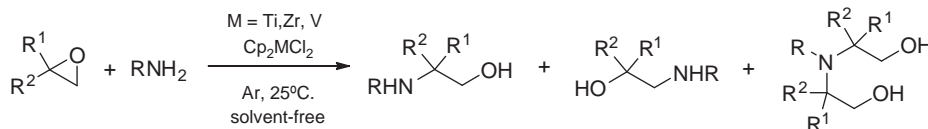
Nilkamal Karelia, Dhimant Desai, Jeremy A. Hengst, Shantu Amin, Sairam V. Rudrabhatla, Jong Yun*

Cancer therapy has moved beyond conventional chemotherapeutics to more mechanism-based targeted approaches. Studies demonstrate that histone deacetylase (HDAC) is a promising target for anticancer agents. Numerous, structurally diverse, hydroxamic acid derivative, HDAC inhibitors have been reported and have been shown to induce growth arrest, differentiation, autophagy, and/or apoptotic cell death by inhibiting multiple signaling pathways in cancer cells. Suberoylanilide hydroxamic acid (SAHA) has emerged as an effective anticancer therapeutic agent and was recently approved by FDA for the treatment of advanced cutaneous T-cell lymphoma. In our previous study, we reported the development of the novel selenium-containing potent HDAC inhibitors, SelSA-1 and SelSA-2. In this study, the effects of SelSA-1 and SelSA-2 on signaling pathways and cytotoxicity were compared with the known HDAC inhibitor, SAHA, in lung cancer cell lines. After 24 h of treatment, SelSA-1 and SelSA-2 inhibited lung cancer cell growth to a greater extent than SAHA in a dose-dependent manner with IC_{50} values at low micromolar concentrations. SelSA-1 and SelSA-2 inhibited ERK and PI3K-AKT signaling pathways while simultaneously increasing in autophagy in A549 cells in a time dependent manner. This preliminary study demonstrates the effectiveness of the selenium-containing analogs of SAHA, SelSA-1, and SelSA-2, as HDAC inhibitors and provides insight into the improvement and/or development of these analogs as a therapeutic approach for the treatment of lung cancer.

**Metallocene catalyzed synthesis of fungistatic vicinal aminoalcohols under solvent free conditions**

pp 6820–6822

Gabriela Mancilla, Rosa M. Durán-Patrón, Antonio J. Macías-Sánchez*, Isidro G. Collado*

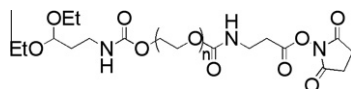


Metallocenes have been evaluated as catalyst in the solvent free, room temperature, preparation of fungistatic vicinal aminoalcohols. The fungistatic activity of the prepared compounds against *Botrytis cinerea* and *Colletotrichum gloeosporioides* is discussed.

Heterobifunctional PEGs: Efficient synthetic strategies and useful conjugation methodologies

pp 6823–6826

Daniel E. Levy*, Brian Frederick, Bing Luo, Samuel Zalipsky*

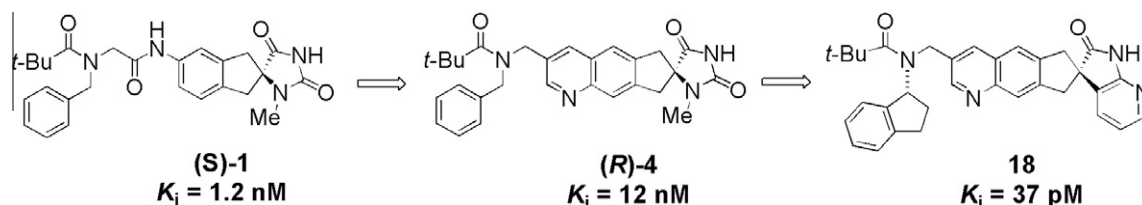


The development of polymeric formulations as drug carriers often requires incorporation of heterobifunctional PEGs capable of sequentially reacting with targeting ligands and structural components of nanoparticles/liposomes. This paper describes efficient syntheses of heterobifunctional PEGs and associated conjugation methodologies.

Novel CGRP receptor antagonists from central amide replacements causing a reversal of preferred chirality

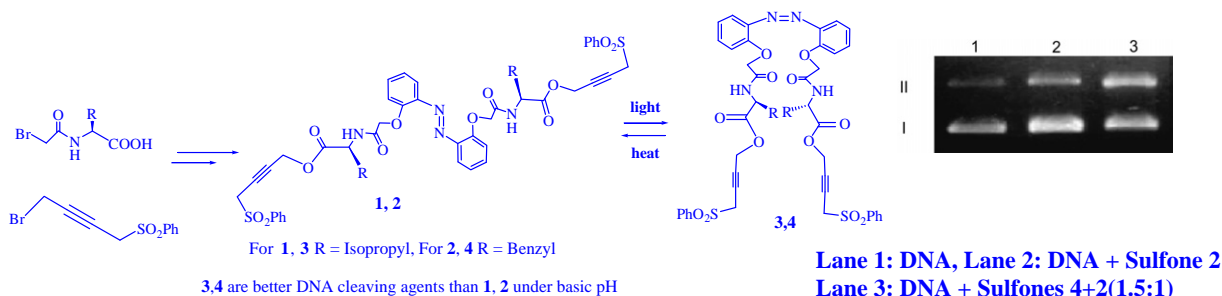
pp 6827–6830

Michael R. Wood, Kathy M. Schirripa, June J. Kim, Rodney A. Bednar, John F. Fay, Joseph G. Bruno, Eric L. Moore, Scott D. Mosser, Shane Roller, Christopher A. Salvatore, Joseph P. Vacca, Harold G. Selnick*

**Design, synthesis and reactivity of C₂-symmetric azobenzene-based amino acid-bis(propargyl sulfones)**

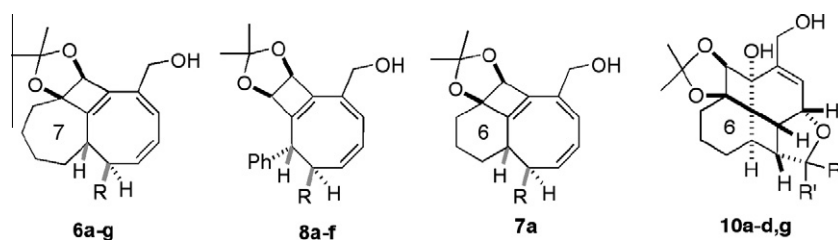
pp 6831–6835

Debarati Mitra, Deb Ranjan Banerjee, Amit Kumar Das, Amit Basak*

**Synthesis of exotic polycycles such as cyclooctatrienes and fenestrenes with differential pro-apoptotic activities on human TRAIL-resistant metastatic cell lines**

pp 6836–6839

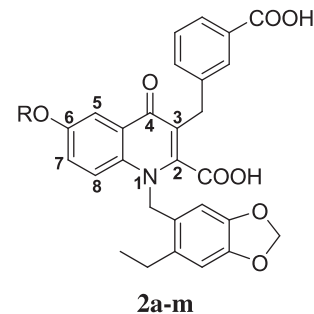
Catherine Hulot, Jean Peluso, Gaëlle Blond, Christian D. Muller*, Jean Suffert*



Synthesis and pharmacological activity of 1,3,6-trisubstituted-4-oxo-1,4-dihydroquinoline-2-carboxylic acids as selective ET_A antagonists

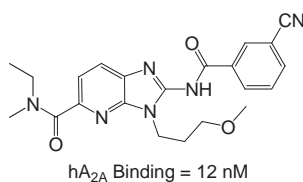
pp 6840–6844

Hardik J. Patel, Nicole Olgun, István Lengyel, Sandra Reznik, Ralph A. Stephani*

The synthesis and structure–activity relationship studies of endothelin A antagonists **2a–m** are reported.**Discovery of 2-aminoimidazopyridine adenosine A_{2A} receptor antagonists**

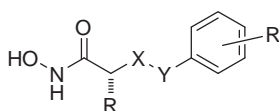
pp 6845–6849

Brian F. McGuinness*, Andrew G. Cole, Guizhen Dong, Marc-Raleigh Brescia, Yuefei Shao, Ian Henderson, Laura L. Rokosz, Tara M. Stauffer, Neelima Mannava, Earl F. Kimble, Catherine Hicks, Nicole White, Pamela G. Wines, Elizabeth Quadros

The synthesis and SAR of a novel series of A_{2A} receptor antagonists are reported.**Antidotes to anthrax lethal factor intoxication. Part 1: Discovery of potent lethal factor inhibitors with in vivo efficacy**

pp 6850–6853

Guan-Sheng Jiao, Seongjin Kim, Mahtab Moayeri, Lynne Cregar-Hernandez, Linda McKasson, Stephen A. Margosiak, Stephen H. Leppla, Alan T. Johnson*



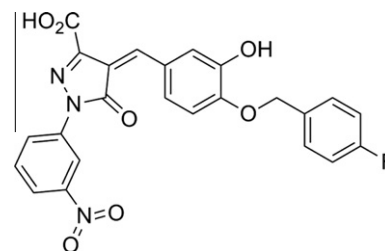
Sub-nanomolar small molecule inhibitors of anthrax lethal factor have been identified.

Development of the next generation of HIV-1 integrase inhibitors: Pyrazolone as a novel inhibitor scaffold

pp 6854–6857

Victor Hadi, Yung-Hyo Koh, Tino Wilson Sanchez, Danielle Barrios, Nouri Neamati*, Kyung Woon Jung*

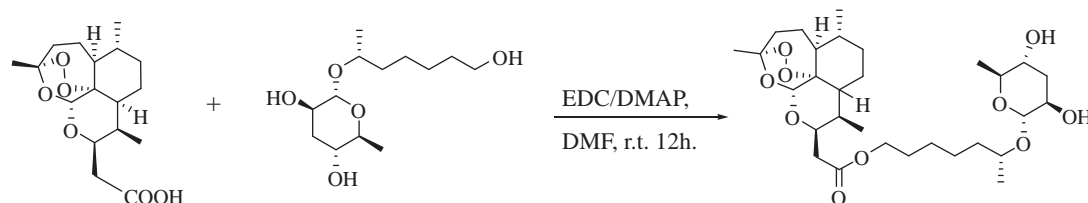
The pyrazolone scaffold, predicted by a computational modeling study using GS-9137(**2**) as a pharmacophoric model, has shown to inhibit the HIV-1 IN activity of 3'-processing and strand transfer process in low micromolar range. We have synthesized various analogs based on the pyrazolone scaffold and performed SAR studies. This paper will showcase the up-to-date result of this scaffold as a promising HIV-1 IN inhibitor.



Concise synthesis and antiangiogenic activity of artemisinin–glycolipid hybrids on chorioallantoic membranes

pp 6858–6860

Jérémy Ricci, Jeehyun Park, Won-Yoon Chung, Kwang-Kyun Park, Mankil Jung*




Novel hybrids of artemisinin–glycolipid were synthesized. Some of these hybrids showed potent *in vivo* antiangiogenic activity that was higher than or comparable to those of fumagillin and thalidomide at a concentration of 2.5 nmol.

**OTHER CONTENTS****Corrigenda**

pp 6861–6864

*Corresponding author

 Supplementary data available via ScienceDirect**COVER**

Overlay of high resolution co-crystal structures of *R*-**22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, 17, 5677.]

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