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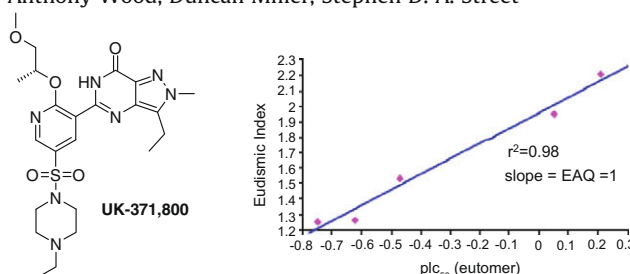
Contents

ARTICLES

Highly potent and selective chiral inhibitors of PDE5: An illustration of Pfeiffer's rule

pp 6033–6036

Mark E. Bunnage*, John P. Mathias, Anthony Wood, Duncan Miller, Stephen D. A. Street



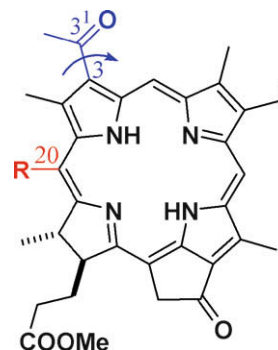
A series of potent and highly-selective chiral PDE5 inhibitors are described, leading to the discovery of clinical candidate **UK-371,800**. Eudismic analysis of this series provides a clear illustration of Pfeiffer's rule.

Rotational deviation of 3-acetyl group from cyclic tetrapyrrole π -plane in synthetic bacteriochlorophyll-*a* analogs by 20-substitution

pp 6037–6040

Hitoshi Tamiaki*, Yuki Kotegawa, Keisuke Mizutani

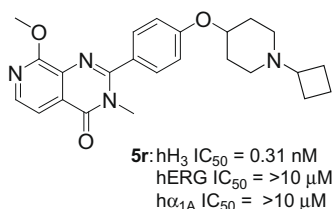
The 3-acetyl group of synthetic methyl pyropheophorbides was rotated around the 3–3¹ bond and the rotational conformers were obtained by 20-bromination and methylation, which affected the redmost Q_y band.



Development of novel 2-[4-(aminoalkoxy)phenyl]-4(3H)-quinazolinone derivatives as potent and selective histamine H₃ receptor inverse agonists

pp 6041–6045

Takashi Mizutani, Tsuyoshi Nagase, Sayaka Ito, Yasuhisa Miyamoto, Takeshi Tanaka, Norihiro Takenaga, Shigeru Tokita, Nagaaki Sato*

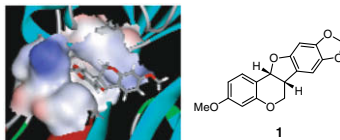


A series of novel 2-[4-(aminoalkoxy)phenyl]-4(3H)-quinazolinone derivatives was discovered as potent human H₃ receptor inverse agonists.

Pterocarpan and flavanones from *Sophora flavescens* displaying potent neuraminidase inhibition

pp 6046–6049

Young Bae Ryu, Marcus J. Curtis-Long, Jin Hyo Kim, Seong Hun Jeong, Min Suk Yang, Keun Woo Lee, Woo Song Lee*, Ki Hun Park*

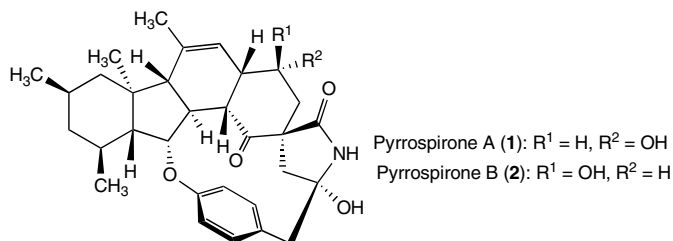


Neuraminidase inhibitory capacity of pterocarpan and flavanones from *Sophora flavescens* was studied. Especially, pterocarpan skeleton was found as a lead structure for neuraminidase inhibitor.

**Pyrrospirones A and B, apoptosis inducers in HL-60 cells, from an endophytic fungus, *Neonectria ramulariae* Wollenw KS-246**

pp 6050–6053

Yoshihito Shiono*, Keiko Shimanuki, Fuminori Hiramatsu, Takuya Koseki, Murayama Tetsuya, Nozomi Fujisawa, Ken-ichi Kimura

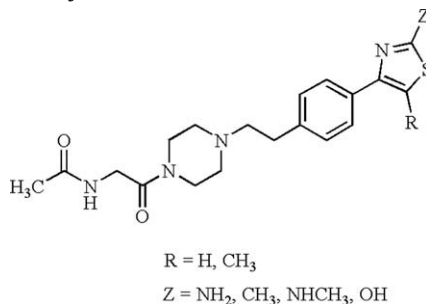


Pyrrospirones A and B have been isolated from the endophytic fungus *Neonectria ramulariae* Wollenw KS-246. The compounds exhibited cytotoxicity and induced apoptosis in human promyelocytic leukemia HL-60 cells.

**Synthesis and preliminary pharmacological evaluation of *N*-2-(4-(2-substitutedthiazol-4-yl)piperazin-1-yl)-2-oxoethyl)acetamides as novel atypical antipsychotic agents**

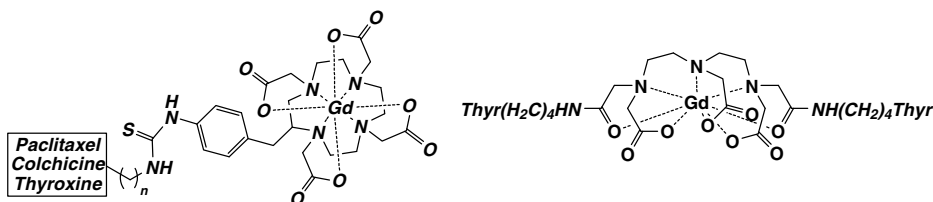
pp 6054–6057

K. V. G. Chandra Sekhar*, V. S. Rao, D. Ravi Kumar Vyas, M. Murali Krishna Kumar

**Synthesis and characterization of novel natural product-Gd(III) MRI contrast agent conjugates**

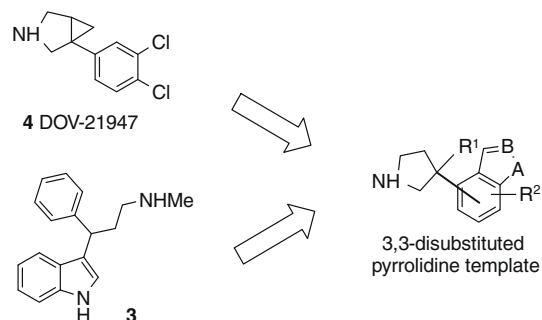
pp 6058–6061

Eleni K. Efthimiadou, Maria E. Katsarou, Michael Fardis, Christos Zikos, Emmanuel N. Pitsinos*, Athanasios Kazantzis, Leondios Leondiadis, Marina Sagnou, Dionisios Vourloumis*

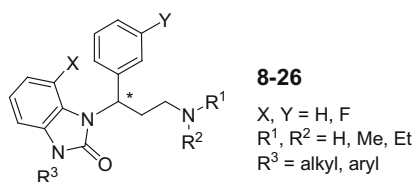


Novel 3,3-disubstituted pyrrolidines as selective triple serotonin/norepinephrine/dopamine reuptake inhibitors pp 6062–6066

Linda M. Bannwart, David S. Carter, Hai-Ying Cai, Jason C. Choy, Robert Greenhouse, Saul Jaime-Figueroa, Pravin S. Iyer, Clara J. Lin, Eun Kyung Lee, Matthew C. Lucas*, Stephen M. Lynch, Ann Marie Madera, Amy Moore, Kerem Ozboya, Lubica Raptova, Ralf Roetz, Ryan C. Schoenfeld, Karin Ann Stein, Sandra Steiner, Marzia Villa, Robert J. Weikert, Yansheng Zhai

**Synthesis and activity of novel 1- or 3-(3-amino-1-phenyl propyl)-1,3-dihydro-2H-benzimidazol-2-ones as selective norepinephrine reuptake inhibitors** pp 6067–6070

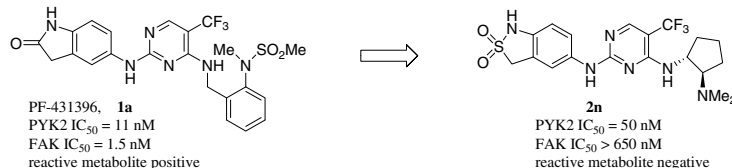
Puwen Zhang*, Eugene A. Terefenko, Casey C. McComas, Paige E. Mahaney, An Vu, Eugene Trybulski, Elizabeth Koury, Grace Johnston, Jenifer Bray, Darlene Deecher



Several compounds from a novel class of 3-(3-amino-1-phenyl propyl)-1,3-dihydro-2H-benzimidazol-2-ones demonstrated potent norepinephrine reuptake inhibition (IC₅₀ 6–25 nM) and excellent selectivity (>100-fold) against serotonin and dopamine uptake transporters.

Trifluoromethylpyrimidine-based inhibitors of proline-rich tyrosine kinase 2 (PYK2): Structure–activity relationships and strategies for the elimination of reactive metabolite formation pp 6071–6077

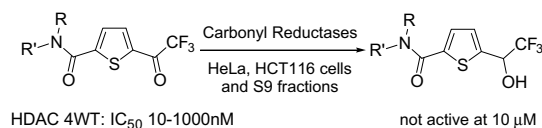
Daniel P. Walker*, F. Christopher Bi, Amit S. Kalgutkar, Jonathan N. Bauman, Sabrina X. Zhao, John R. Soglia, Gary E. Aspnes, Daniel W. Kung, Jacquelyn Klug-McLeod, Michael P. Zawistoski, Molly A. McGlynn, Robert Oliver, Matthew Dunn, Jian-Cheng Li, Daniel T. Richter, Beth A. Cooper, John C. Kath, Catherine A. Hulford, Christopher L. Autry, Michael J. Luzzio, Ethan J. Ung, W. Gregory Roberts, Peter C. Bonnette, Leonard Buckbinder, Anil Mistry, Matthew C. Griffor, Seungil Han, Angel Guzman-Perez



Synthesis and structure–activity relationships for a series of diaminopyrimidines as proline-rich tyrosine kinase (PYK2) inhibitors are described. Strategies for the elimination of reactive metabolite formation within this chemical series are also described.

Studies of the metabolic stability in cells of 5-(trifluoroacetyl)thiophene-2-carboxamides and identification of more stable class II histone deacetylase (HDAC) inhibitors pp 6078–6082

Rita Scarpelli*, Annalise Di Marco, Federica Ferrigno, Ralph Laufer, Isabella Marcucci, Ester Muraglia, Jesus M. Ontoria, Michael Rowley, Sergio Serafini, Christian Steinkühler, Philip Jones

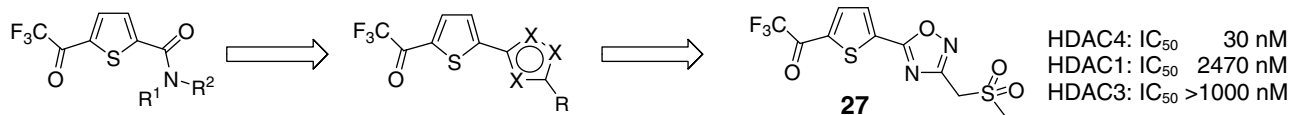


The cause for the lack of cellular activity of the 5-(trifluoroacetyl)-thiophene-2-carboxamides was investigated. A rapid screening assay identified analogs as potent, selective, and metabolically stable class II HDAC inhibitors.

2-Trifluoroacetylthiophene oxadiazoles as potent and selective class II human histone deacetylase inhibitors

pp 6083–6087

Ester Muraglia*, Sergio Altamura, Danila Branca, Ottavia Cecchetti, Federica Ferrigno, Maria Vittoria Orsale, Maria Cecilia Palumbi, Michael Rowley, Rita Scarpelli, Christian Steinkühler, Philip Jones



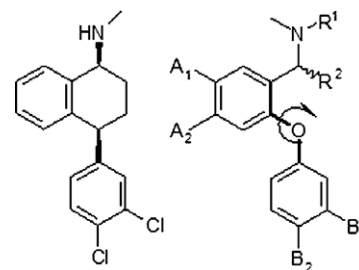
Replacement of the carboxamide moiety of trifluoroacetylthiophene HDAC4 inhibitors with bioisosteric pentatomic heteroaromatics led to the discovery of a novel series of potent and highly selective low nanomolar class II HDAC inhibitors.

Quantitative structure–activity relationship of phenoxyphenyl-methanamine compounds with 5HT_{2A}, SERT, and hERG activities

pp 6088–6092

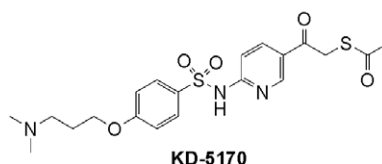
Scot Mente*, Randall Gallaschun, Anne Schmidt, Lorrie Lebel, Michelle Vanase-Frawley, Anton Fliri

QSAR models have been used to evaluate activities for compounds in the phenoxyphenyl-methanamine (PPMA) class of compounds. These models utilize Hammett-type donating–withdrawing substituent values as well as simple parameters to describe substituent size and elucidate the SAR of the 'A' and 'B' rings. Using this methodology, intuitive QSAR relationships were found for the three biological activities with *R*² values of 0.73, 0.45, and 0.58 for 5HT_{2A}, SerT, and hERG activities.

**Identification of KD5170: A novel mercaptoketone-based histone deacetylase inhibitor**

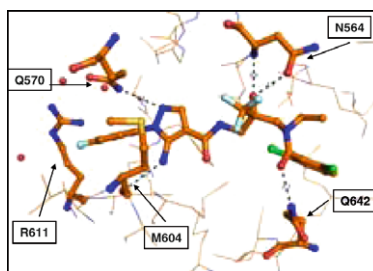
pp 6093–6096

Joseph E. Payne, Céline Bonnefous, Christian A. Hassig, Kent T. Symons, Xin Guo, Phan-Manh Nguyen, Tami Annable, Paul L. Wash, Timothy Z. Hoffman, Tadimeti S. Rao, Andrew K. Shiau, James W. Malecha, Stewart A. Noble, Jeffrey H. Hager, Nicholas D. Smith*

**The first X-ray crystal structure of the glucocorticoid receptor bound to a non-steroidal agonist**

pp 6097–6099

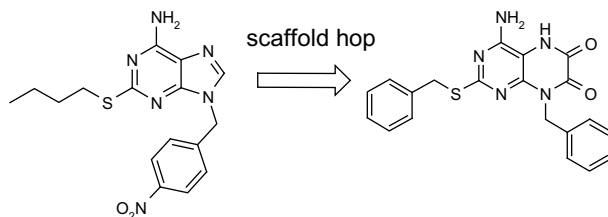
Kevin P. Madauss*, Randy K. Bledsoe, Iain Mclay, Eugene L. Stewart, Iain J. Uings, Gordon Weingarten, Shawn P. Williams



The X-ray crystal structure of **1** in the GR ligand-binding domain is reported.

Exploring 8-benzyl pteridine-6,7-diones as inhibitors of glutamate racemase (Murl) in Gram-positive bacteria pp 6100–6103

Gloria A. Breault*, Janelle Comita-Prevoir, Charles J. Eyermann, Bolin Geng, Randy Petrichko, Peter Doig, Elise Gorseth, Brian Noonan

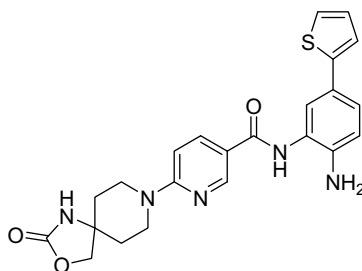


A successful scaffold-hopping approach gave a novel series of inhibitors of bacterial glutamate racemase (Murl). Early SAR studies of the 8-benzyl pteridine-6,7-diones led to compounds with micromolar enzyme potency and antibacterial activity.

SAR profiles of spirocyclic nicotinamide derived selective HDAC1/HDAC2 inhibitors (SHI-1:2)

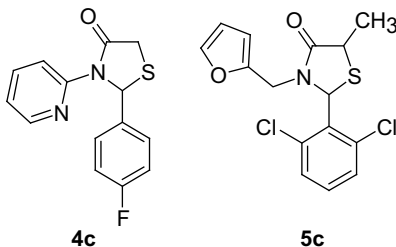
pp 6104–6109

Joey L. Methot*, Christopher L. Hamblett, Dawn M. Mampreian, Joon Jung, Andreas Harsch, Alexander A. Szewczak, William K. Dahlberg, Richard E. Middleton, Bethany Hughes, Judith C. Fleming, Hongmei Wang, Astrid M. Kral, Nicole Ozerova, Jonathan C. Cruz, Brian Haines, Melissa Chenard, Candia M. Kenific, J. Paul Secrist, Thomas A. Miller

**Non-nucleoside inhibitors of the hepatitis C virus NS5B RNA-dependant RNA polymerase: 2-Aryl-3-heteroaryl-1,3-thiazolidin-4-one derivatives**

pp 6110–6114

Ravindra K. Rawal, S. B. Katti*, Neerja Kaushik-Basu, Payal Arora, Zhenhua Pan

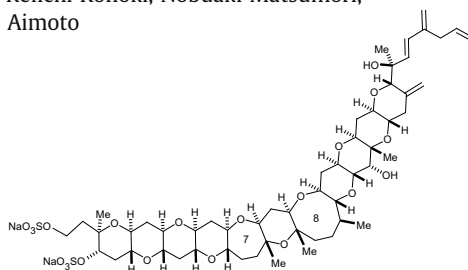


A library of 4-thiazolidinones was evaluated for their ability to inhibit HCV NS5B. The two most active compounds **4c** and **5c** exhibited an IC_{50} of 31.9 μ M and 32.2 μ M, respectively, against HCV NS5B.

**Interaction of ladder-shaped polyethers with transmembrane α -helix of glycoporphin A as evidenced by saturation transfer difference NMR and surface plasmon resonance**

pp 6115–6118

Satoru Ujihara, Tohru Oishi*, Kohei Torikai, Keiichi Konoki, Nobuaki Matsumori, Michio Murata*, Yasukatsu Oshima, Saburo Aimoto

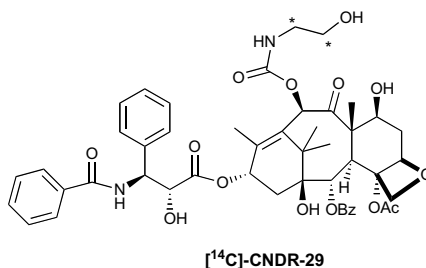


Saturation transfer difference NMR spectra revealed that yessotoxin interacts with glycoporphin A with a polyene side chain and angular methyl groups.

In situ blood–brain barrier permeability of a C-10 paclitaxel carbamate

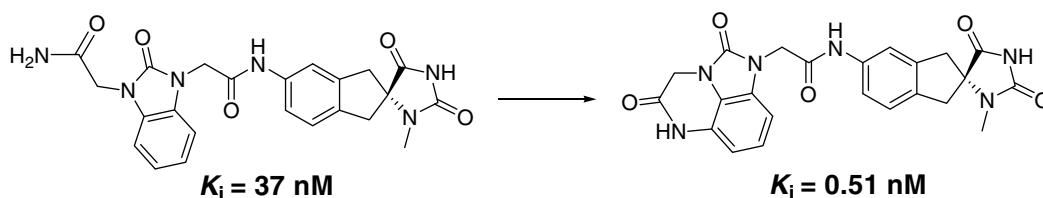
pp 6119–6121

Carlo Ballatore*, Bin Zhang, John Q. Trojanowski, Virginia M.-Y. Lee, Amos B. Smith III

**Potent benzimidazolone-based CGRP receptor antagonists**

pp 6122–6125

Cory R. Theberge*, Rodney A. Bednar, Ian M. Bell, Halea A. Corcoran, John F. Fay, James C. Hershey, Victor K. Johnston, Stefanie A. Kane, Scott Mosser, Christopher A. Salvatore, Theresa M. Williams, C. Blair Zartman, Xu-Fang Zhang, Samuel L. Graham, Joseph P. Vacca

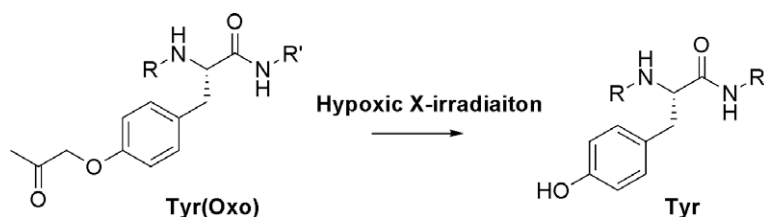


Elaboration of the benzimidazolone core of spirohydantoin CGRP receptor antagonists is described.

Radiolytic one-electron reduction characteristics of tyrosine derivative caged by 2-oxopropyl group

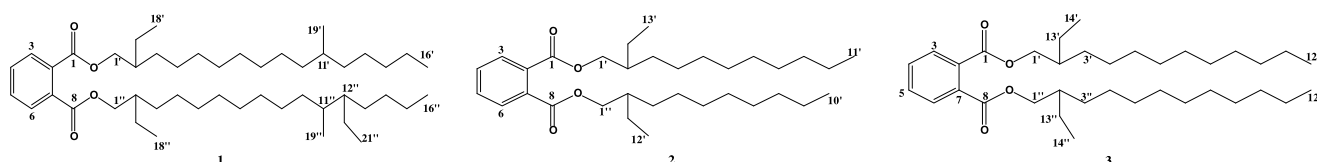
pp 6126–6129

Kazuhito Tanabe*, Masahiko Ebihara, Nao Hirata, Sei-ichi Nishimoto*

**Cathepsin B inhibitory activities of three new phthalate derivatives isolated from seahorse, *Hippocampus Kuda Bleeler***

pp 6130–6134

Yong Li, Zhong-Ji Qian, Se-Kwon Kim*

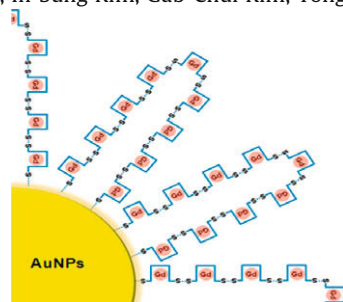


Three new phthalate acid derivatives, 2,12-diethyl-11-methylhexadecyl 2-ethyl-11-methylhexadecyl phthalate (**1**), 2-ethyldecyl 2-ethylundecyl phthalate (**2**), and bis(2-ethylundecyl) phthalate (**3**), were isolated from seahorse, *Hippocampus Kuda Bleeler*, together with a known natural analog bis(2-ethylheptyl) phthalate (**4**). The four phthalate derivatives showed dose-dependent cathepsin B inhibitions activities with IC_{50} values of 0.13 mM (**1**), 0.21 mM (**2**), 0.18 mM (**3**), and 0.29 mM (**4**), respectively.

Gold nanoparticles functionalised by Gd-complex of DTPA-bis(amide) conjugate of glutathione as an MRI contrast agent

pp 6135–6137

Ji-Ae Park, Pattubala A. N. Reddy, Hee-Kyung Kim, In-Sung Kim, Gab-Chul Kim, Yongmin Chang*, Tae-Jeong Kim*

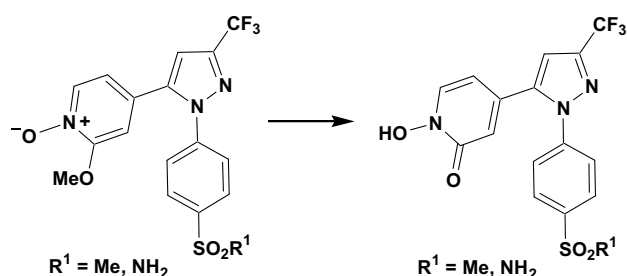


The synthesis and relaxivity properties of Gd-complex coated gold nanoparticles are reported.

**Synthesis of celecoxib analogs that possess a *N*-hydroxypyrid-2(1*H*)one 5-lipoxygenase pharmacophore: Biological evaluation as dual inhibitors of cyclooxygenases and 5-lipoxygenase with anti-inflammatory activity**

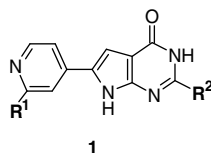
pp 6138–6141

Morshed Alam Chowdhury, Khaled R. A. Abdellatif, Ying Dong, Dipankar Das, Mavanur R. Suresh, Edward E. Knaus*

**Pyrrolo-pyrimidones: A novel class of MK2 inhibitors with potent cellular activity**

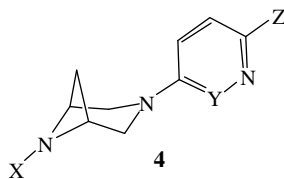
pp 6142–6146

Achim Schlapbach*, Roland Feifel, Stuart Hawtin, Richard Heng, Guido Koch, Henrik Moebitz, Laszlo Revesz, Clemens Scheufler, Juraj Velcicky, Rudolf Waelchli, Christine Huppertz

Pyrrolo-pyrimidones of the general structure **1** were synthesized and evaluated for their potential as MK2 inhibitors.**Synthesis of 3,6-diazabicyclo[3.1.1]heptanes as novel ligands for neuronal nicotinic acetylcholine receptors**

pp 6147–6150

Gabriele Murineddu*, Caterina Murruzzu, Maria M. Curzu, Giorgio Chelucci, Cecilia Gotti, Annalisa Gaimarri, Laura Legnani, Lucio Toma, Gerard A. Pinna



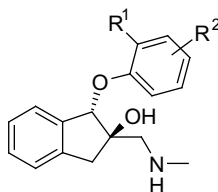
- X = H, Y = CH, Z = Cl (**a**)
 X = H, Y = CH, Z = H (**b**)
 X = H, Y = CH, Z = Br (**c**)
 X = H, Y = CH, Z = NO₂ (**d**)
 X = H, Y = N, Z = Cl (**e**)
 X = CH₃, Y = CH, Z = Cl (**f**)

A series of novel pyridyl 3,6-diazabicyclo[3.1.1]heptane (**4a–f**) $\alpha 4\beta 2$ ligands was identified. SAR around pyridine moiety resulted in the discovery of compounds with affinities in the low nanomolar range.

Synthesis and structure–activity relationships of selective norepinephrine reuptake inhibitors (sNRI) with improved pharmaceutical characteristics

pp 6151–6155

Joseph Pontillo, Dongpei Wu, Brett Ching, Sarah Hudson, Marc J. Genicot, Yinghong Gao, Todd Ewing, Beth A. Fleck, Kathleen Gogas, Anna Aparicio, Hua Wang, Jenny Wen, Warren S. Wade*



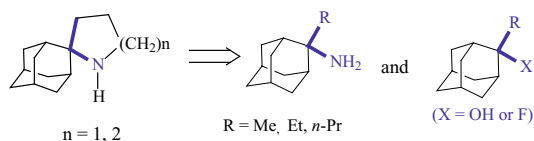
Norepinephrine reuptake inhibitors with improved physicochemical properties are described. Typical compound are potent ($IC_{50}s < 10$ nM), selective, weak CYP2D6 inhibitors ($IC_{50}s > 1$ μ M) and resistant to oxidation by human liver microsomes, with a favorable polarity profile.



Comparisons of the influenza virus A M2 channel binding affinities, anti-influenza virus potencies and NMDA antagonistic activities of 2-alkyl-2-aminoadamantanes and analogues

pp 6156–6160

Antonios Kolocouris*, Philip Spearpoint, Stephen R. Martin, Alan J. Hay, Marta López-Querol, Francesc X. Sureda, Elizaveta Padalko, Johan Neyts, Erik De Clercq

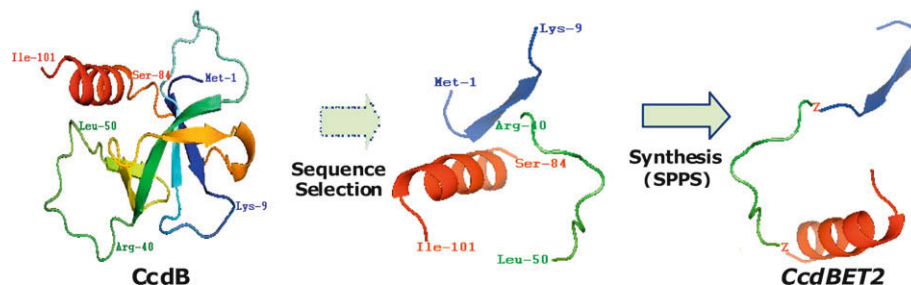


The M2 binding affinities, anti-influenza virus potencies and NMDA antagonist activities of some aminoadamantane derivatives and analogues were evaluated. The data can be used for mapping the influenza virus A M2 channel lipophilic pocket. Some important lead structures for drug design purposes emerged.

Peptides based on CcdB protein as novel inhibitors of bacterial topoisomerases

pp 6161–6164

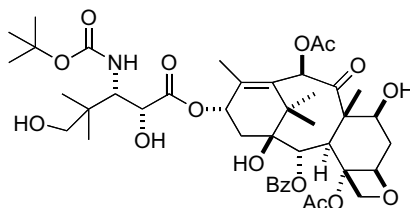
Eliane Trovatti, Camila A. Cotrim, Saulo S. Garrido, Ronaldo S. Barros, Reinaldo Marchetto*



Synthesis, tubulin assembly, and antiproliferative activity against MCF7 and NCI/ADR-RES cancer cells of 10-O-acetyl-5'-hydroxybutitaxel

pp 6165–6167

Haibo Ge, Jianmei Wang, Margaret M. Kayser, Richard H. Himes, Gunda I. Georg*

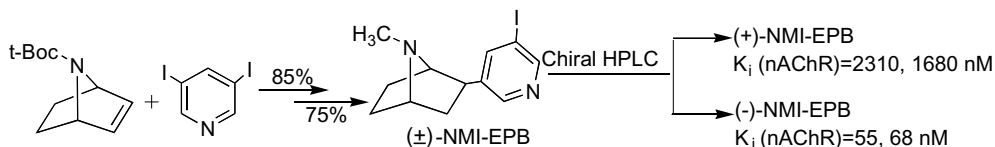


A highly efficient kinetic resolution of racemic cis-4-(2-*tert*-butyldimethylsilyloxy-1,1-dimethyl)ethyl-3-*tert*-butyldimethylsilyloxy-azetidin-2-one with 7-O-triethylsilylbaccatin III was carried out to furnish 10-O-acetyl-5'-hydroxybutitaxel after removal of the silyl protecting groups. The compound was 50% as active as paclitaxel in a tubulin assembly assay and showed significantly decreased activity against MCF7 cell proliferation compared to paclitaxel.

New synthesis and evaluation of enantiomers of 7-methyl-2-*exo*-(3'-iodo-5'-pyridinyl)-7-azabicyclo[2.2.1]heptane as stereoselective ligands for PET imaging of nicotinic acetylcholine receptors

pp 6168–6170

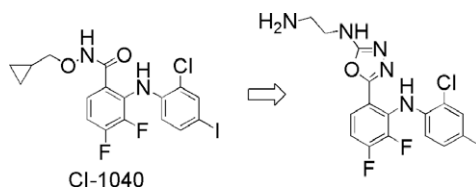
Yongjun Gao*, Andrew G. Horti, Hiroto Kuwabara, Hayden T. Ravert, Daniel P. Holt, Anil Kumar, Mohab Alexander, Dean F. Wong, Robert F. Dannals



2-Alkylamino- and alkoxy-substituted 2-amino-1,3,4-oxadiazoles—O-Alkyl benzohydroxamate esters replacements retain the desired inhibition and selectivity against MEK (MAP ERK kinase)

pp 6171–6174

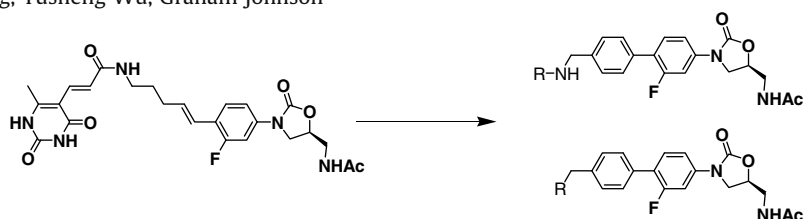
Joseph S. Warmus*, Cathlin Flamme, Lu Yan Zhang, Stephen Barrett, Alexander Bridges, Huifen Chen, Richard Gowan, Michael Kaufman, Judy Sebolt-Leopold, Wilbur Leopold, Ronald Merriman, Jeffrey Ohren, Alexander Pavlovsky, Sally Przybranowski, Haile Tecle, Heather Valik, Christopher Whitehead, Erli Zhang



Design at the atomic level: Design of biaryloxazolidinones as potent orally active antibiotics

pp 6175–6178

Jiacheng Zhou, Ashoke Bhattacharjee, Shili Chen, Yi Chen, Erin Duffy, Jay Farmer, Joel Goldberg, Roger Hanselmann, Joseph A. Ippolito, Rongliang Lou, Alia Orbin, Ayomi Oyeler, Joe Salvino, Dane Springer, Jennifer Tran, Deping Wang, Yusheng Wu, Graham Johnson*

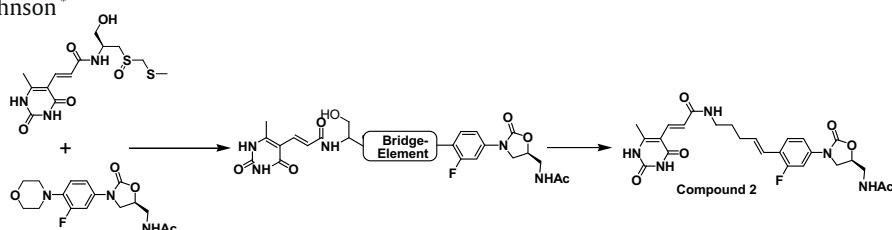


We have developed a first generation of hybrid sparsomycin–linezolid compounds into a new family of orally bioavailable biaryloxazolidinones that have activity against both linezolid-susceptible and -resistant Gram-positive bacteria as well as the fastidious Gram-negative bacteria *Haemophilus influenzae* and *Moraxella catarrhalis*. The convergent synthesis of these new compounds is detailed.

Design at the atomic level: Generation of novel hybrid biaryloxazolidinones as promising new antibiotics

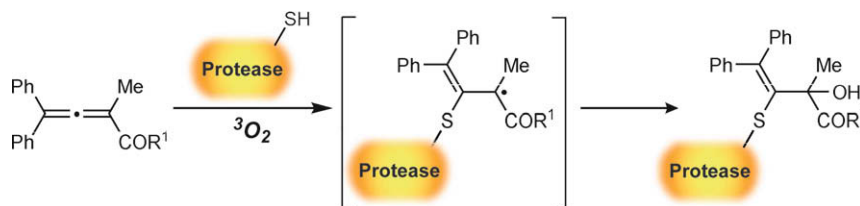
pp 6179–6183

Jiacheng Zhou, Ashoke Bhattacharjee, Shili Chen, Yi Chen, Erin Duffy, Jay Farmer, Joel Goldberg, Roger Hanselmann, Joseph A. Ippolito, Rongliang Lou, Alia Orbin, Ayomi Oyeler, Joe Salvino, Dane Springer, Jennifer Tran, Deping Wang, Yusheng Wu, Graham Johnson*

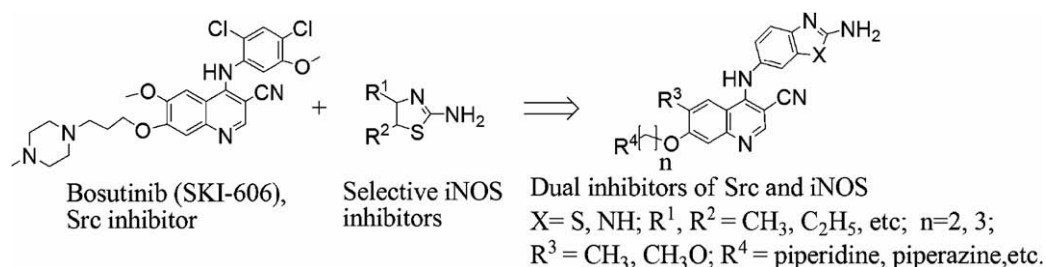


From the X-ray crystal structures of linezolid and the non-selective antibiotic sparsomycin, we have derived a new family of hybrid oxazolidinones. From this initial compound set we have developed a new biaryloxazolidinone scaffold that shows both potent antimicrobial activity as well as selective inhibition of ribosomal translation. The synthesis of these compounds is outlined.

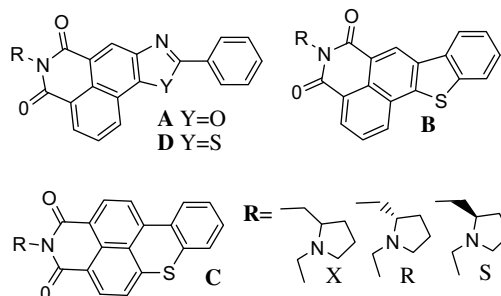
Yoshio Takeuchi*, Tomoya Fujiwara, Yoshihito Shimone, Hideki Miyataka, Toshio Satoh, Kenneth L. Kirk, Hitoshi Hori



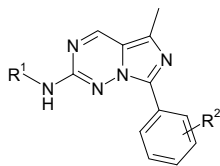
Xin Cao, Qi-Dong You*, Zhi-Yu Li, Xiao-Rong Liu, Dan Xu, Qing-Long Guo, Jing Shang, Ji-Wang Chern, Meng-Ling Chen



Qing Yang*, Peng Yang, Xuhong Qian*, Lianpeng Tong



M. Cheung*, K. W. Kuntz, M. Pobanz, J. M. Salovich, B. J. Wilson, C. W. Andrews III, L. M. Shewchuk, A. H. Epperly, D. F. Hassler, M. A. Leesnitzer, J. L. Smith, G. K. Smith, T. J. Lansing, R. A. Mook Jr.

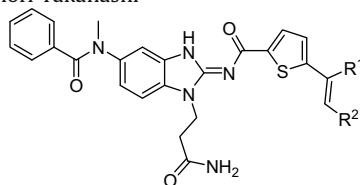


The synthesis and biological activities of imidazo[5,1-f][1,2,4]triazin-2-amines (imidazotriazines) as novel polo-like kinase 1 inhibitors are reported.

2-Aminobenzimidazoles as potent ITK antagonists: *trans*-stilbene-like moieties targeting the kinase specificity pocket

pp 6218–6221

Ho Yin Lo*, Jörg Bentzien, Roman W. Fleck, Steven S. Pullen, Hnin Hnin Khine, Joseph R. Woska Jr., Stanley Z. Kugler, Mohammed A. Kashem, Hidenori Takahashi



$R^1 = \text{H or CH}_3$

$R^2 = \text{H, CN, COOMe, aromatics and heterocycles}$

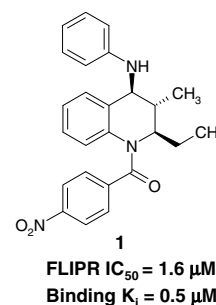
The design and syntheses of a series of *trans*-stilbene-like ITK antagonists were described.

Tetrahydro-4-quinolinamines identified as novel P2Y₁ receptor antagonists

pp 6222–6226

Ángel I. Morales-Ramos*, John S. Mecom, Terry J. Kiesow, Todd L. Graybill, Gregory D. Brown, Nambi V. Aiyar, Elizabeth A. Davenport, Lorena A. Kallal, Beth A. Knapp-Reed, Peng Li, Allyn T. Londregan, Dwight M. Morrow, Shobha Senadhi, Reema K. Thalji, Steve Zhao, Cynthia L. Burns-Kurtis, Joseph P. Marino Jr.*

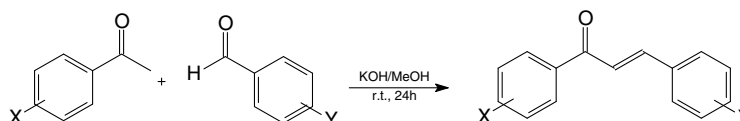
High-throughput screening of the GSK compound collection against the P2Y₁ receptor identified a novel series of tetrahydro-4-quinolinamine antagonists. Optimal substitution around the piperidine group was pivotal for ensuring activity. An exemplar analog from this series was shown to inhibit platelet aggregation.



Synthetic chalcones as efficient inhibitors of *Mycobacterium tuberculosis* protein tyrosine phosphatase PtpA

pp 6227–6230

Louise Domeneghini Chiaradia, Alessandra Mascarello, Marcela Purificação, Javier Vernal, Marlon Norberto Sechini Cordeiro, Maria Emilia Zenteno, Andréa Villarino, Ricardo José Nunes, Rosendo Augusto Yunes, Hernán Terenzi*



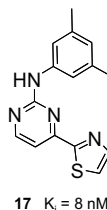
In the search for lead compounds for new drugs for tuberculosis, the activity of 38 synthetic chalcones were assayed for their potential inhibitory action towards a protein tyrosine phosphatase from *Mycobacterium tuberculosis* – PtpA.



Discovery and SAR of novel 4-thiazolyl-2-phenylaminopyrimidines as potent inhibitors of spleen tyrosine kinase (SYK)

pp 6231–6235

Luc J. Farmer*, Guy Bemis, Shawn D. Britt, John Cochran, Martin Connors, Edmund M. Harrington, Thomas Hoock, William Markland, Suganthini Nanthakumar, Paul Taslimi, Ernst Ter Haar, Jian Wang, Darshana Zhaveri, Francesco G. Salituro

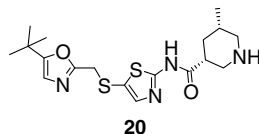


The synthesis of potent novel SYK inhibitors such as **17** (K_i = 8 nM) is reported.

Modifications of the isonipecotic acid fragment of SNS-032: Analogs with improved permeability and lower efflux ratio

pp 6236–6239

Junfa Fan^{*}, Bruce Fahr, David Stockett, Erica Chan, Sravanthi Cheeti, Iana Serafimova, Yafan Lu, Phuongly Pham, Duncan H. Walker, Ute Hoch^{*}, Ingrid C. Choong^{*}

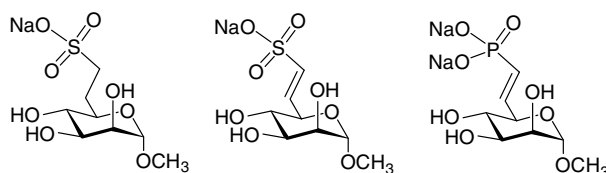


The identification of a selective CDK2, 7, 9 inhibitor **20** with improved permeability is described. The synthesis and in vitro properties of **20** are discussed.

Synthesis of new sulfonate and phosphonate derivatives for cation-independent mannose 6-phosphate receptor targeting

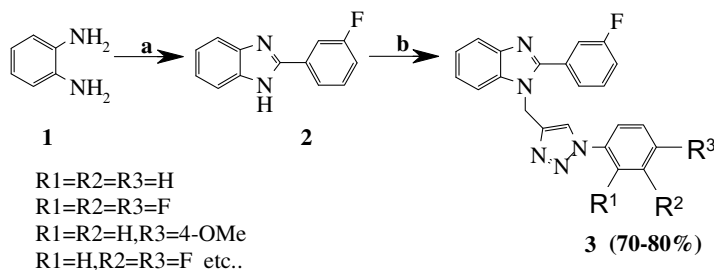
pp 6240–6243

Audrey Jeanjean, Magali Gary-Bobo, Philippe Nirdé, Simon Leiris, Marcel Garcia, Alain Morère^{*}

**Clubbed [1,2,3] triazoles by fluorine benzimidazole: A novel approach to H37Rv inhibitors as a potential treatment for tuberculosis**

pp 6244–6247

Charansingh Gill^{*}, Ganesh Jadhav, Mohammad Shaikh, Rajesh Kale, Anant Ghawalkar, Deepak Nagargoje, Mahendra Shiradkar

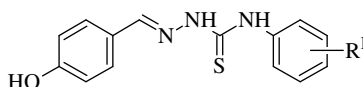


a: 3-Fluoro benzaldehyde, Toluene, 110 °C; **b:** NaH, Substituted [1,2,3] triazole, DMF, RT

Synthesis and Ribonucleotide reductase inhibitory activity of thiosemicarbazones

pp 6248–6250

Kesavan Krishnan, Kumari Prathiba, Venkatesan Jayaprakash^{*}, Arijit Basu, Nibha Mishra, Bingsen Zhou, Shuya Hu, Yun Yen^{*}



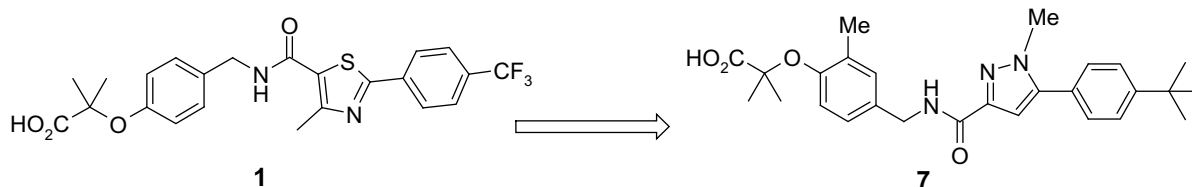
Twenty-one new thiosemicarbazone derivatives were synthesized and screened for Ribonucleotide reductase (RR) inhibitory activity against recombinant human RR subunits, hRRM1 and hRRM2, by holoenzyme-based [³H]CDP reduction in vitro assay. *p*-Hydroxy benzaldehyde-derived thiosemicarbazones, **17–27**, were more potent than Hydroxyurea (**HU**).



The discovery of equipotent PPAR α / γ dual activators

pp 6251–6254

Paul Martres*, Nicolas Faucher, Alain Laroze, Olivier Pineau, Marie Helene Fouchet, Florent Potvain, Didier Grillot, Veronique Beneton

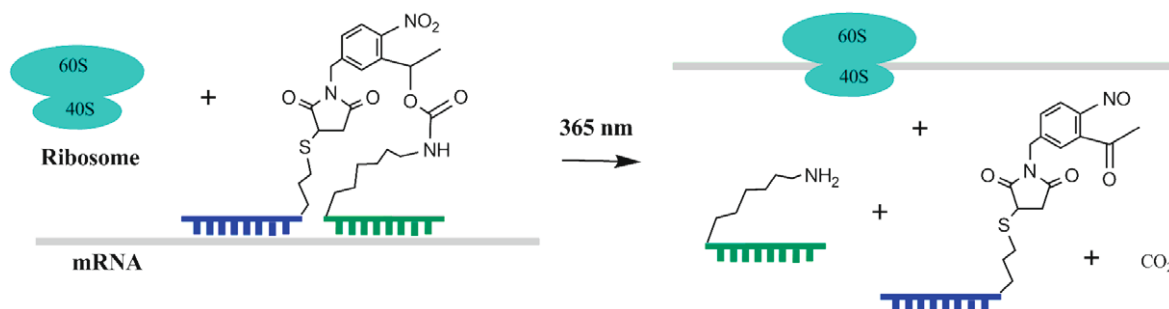


We report the design and synthesis of equipotent PPAR α / γ dual agonists starting from the selective PPAR α agonist **1**. In vivo data for **7** in the Zucker fa/fa rat are presented.

**RNA bandages for photoregulating in vitro protein synthesis**

pp 6255–6258

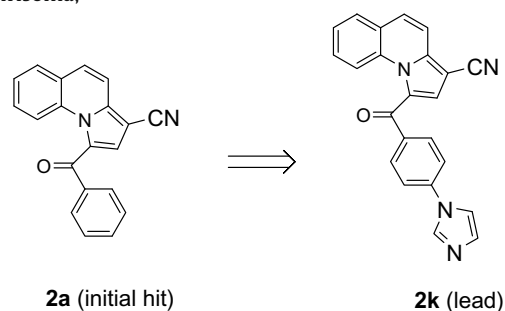
Julia L. Richards, XinJing Tang, Anna Turetsky, Ivan J. Dmochowski*

**Discovery of 1-benzoyl-3-cyanopyrrolo[1,2-a]quinolines as a new series of apoptosis inducers using a cell- and caspase-based high-throughput screening assay. Part 1: Structure–activity relationships of the 1- and 3-positions**

pp 6259–6264

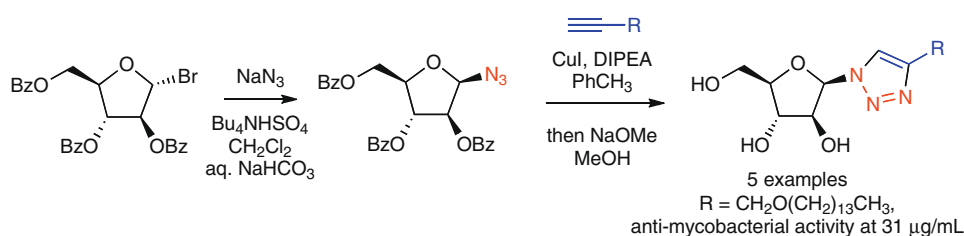
William Kemnitzer, Jared Kuemmerle, Songchun Jiang, Han-Zhong Zhang, Nilantha Sirisoma, Shailaja Kasibhatla, Candace Crogan-Grundy, Ben Tseng, John Drewe, Sui Xiong Cai*

The discovery and SAR studies of a series of apoptosis inducing 1-benzoyl-3-cyanopyrrolo [1,2-a]quinolines with modifications at the 1- and 3-positions is reported.

**2a** (initial hit)**2k** (lead)**Synthesis of Arabino glycosyl triazoles as potential inhibitors of mycobacterial cell wall biosynthesis**

pp 6265–6267

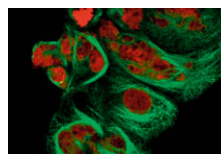
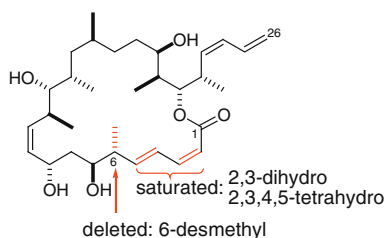
Brendan L. Wilkinson, Hilary Long, Edith Sim, Antony J. Fairbanks*



Total synthesis and biological evaluation of potent analogues of dictyostatin: Modification of the C2–C6 dienolate region

pp 6268–6272

Ian Paterson*, Nicola M. Gardner, Esther Guzmán, Amy E. Wright



PANC-1 after 100 nM incubation with 6-desmethyldictyostatin

6-Desmethyldictyostatin and 2,3-dihydrodictyostatin displayed low nanomolar antiproliferative activity in Taxol-sensitive and resistant cell lines, intermediate between dictyostatin and discodermolide, while 2,3,4,5-tetrahydrodictyostatin showed activity comparable to discodermolide.

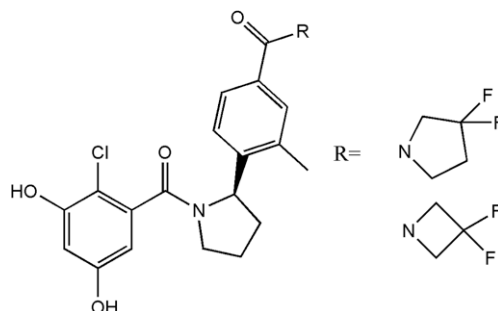


Dihydroxyphenyl amides as inhibitors of the Hsp90 molecular chaperone

pp 6273–6278

Pei-Pei Kung*, Lee Funk, Jerry Meng, Michael Collins, Joe Zhongxiang Zhou, M. Catherine Johnson, Anne Ekker, Jeff Wang, Pramod Mehta, Min-Jean Yin, Caroline Rodgers, Jay F. Davies II, Eileen Bayman, Tod Smeal, Karen A. Maegley, Michael R. Gehring

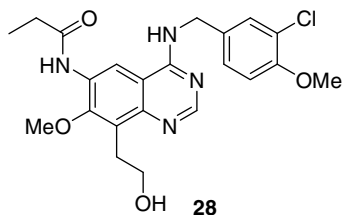
A series of dihydroxyphenyl amides as Hsp90 inhibitor was discovered from a HTS hit using structure based design and library synthesis techniques.



Quinazolines as potent and highly selective PDE5 inhibitors as potential therapeutics for male erectile dysfunction

pp 6279–6282

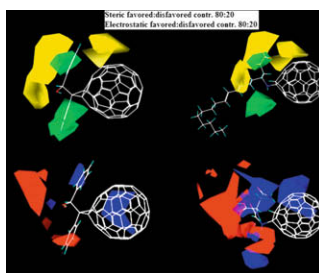
Young Hoon Kim, Hojin Choi, Jaekwang Lee, In-Chang Hwang, Seung Kee Moon, Soo Jin Kim, Hong Woo Lee, Dai Sig Im, Sung Sook Lee, Soon Kil Ahn, Sang Woong Kim, Cheol Kyu Han, Jeong Hyeok Yoon, Kyung Joo Lee*, Nam Song Choi*



3D QSAR CoMFA/CoMSIA, molecular docking and molecular dynamics studies of fullerene-based HIV-1 PR inhibitors

pp 6283–6289

Serdar Durdagi*, Thomas Mavromoustakos, Manthos G. Papadopoulos*



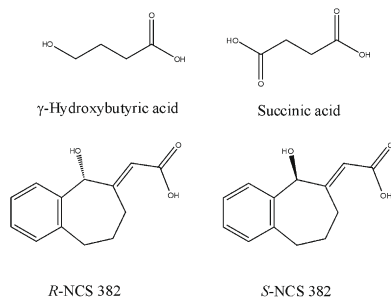
For the first time, a set of experimentally reported [60] fullerene derivatives were subjected 3D-QSAR studies by employing the CoMFA and CoMSIA methodologies. The aim of this study is to propose a series of novel [60] fullerene-based inhibitors with optimal binding affinity for the HIV-1 PR enzyme.



Validation of high-affinity binding sites for succinic acid through distinguishable binding of gamma-hydroxybutyric acid receptor-specific NCS 382 antipodes

pp 6290–6292

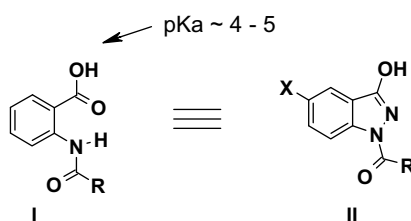
Tünde Molnár*, Júlia Visy, Ágnes Simon, István Moldvai, Eszter Temesvári-Major, Gábor Dörnyei, Erzsébet Kútiné Fekete, Julianna Kardos



Bacterial translation inhibitors, 1-acylindazol-3-ols as anthranilic acid mimics

pp 6293–6297

Cory Stiff, David R. Graber, Atli Thorarensen, Brian D. Wakefield, Keith R. Marotti, Earline P. Melchior, Michael T. Sweeney, Fusen Han, Douglas C. Rohrer, Gary E. Zurenko, Donna L. Romero*



This paper describes the discovery of 1-acylindazol-3-ols as a novel bioisostere of an anthranilic acid. The synthesis and structure–activity relationships of the indazol bioisosteres are described herein.

OTHER CONTENTS

Instructions to contributors

p I

*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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