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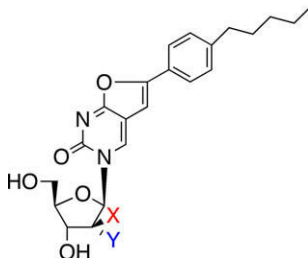
Bioorganic & Medicinal Chemistry Letters Volume 19, Issue 22, 2009

Contents

ARTICLES

2'-Fluorosugar analogues of the highly potent anti-varicella-zoster virus bicyclic nucleoside analogue (BCNA) Cf 1743 pp 6264–6267

Christopher McGuigan^{*}, Marco Derudas, Maurizio Quintiliani, Graciela Andrei, Robert Snoeck, Geoffrey Henson, Jan Balzarini

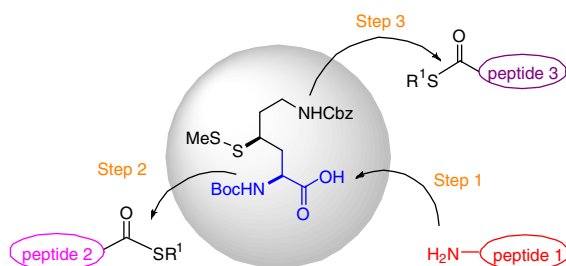


Only the beta fluoro analogue (X = F, Y = H) retains potent anti-VZV activity.



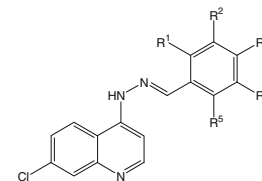
Synthesis of 4-mercapto-L-lysine derivatives: Potential building blocks for sequential native chemical ligation pp 6268–6271

Kalyan Kumar Pasunooti, Renliang Yang, Seenuvasan Vedachalam, Bala Kishan Gorityala, Chuan-Fa Liu^{*}, Xue-Wei Liu^{*}



Synthesis and antitubercular activity of 7-chloro-4-quinolinyhydrazone derivatives pp 6272–6274

André L. P. Candéa, Marcelle de L. Ferreira, Karla C. Pais, Laura N. de F. Cardoso, Carlos R. Kaiser, Maria das Graças M. de O. Henriques, Maria C. S. Lourenço, Flávio A. F. M. Bezerra, Marcus V. N. de Souza^{*}



3a-u
R¹ = X; R² = R³ = R⁴ = R⁵ = H
R² = X; R¹ = R³ = R⁴ = R⁵ = H
R³ = X; R¹ = R² = R⁴ = R⁵ = H
X = H; Cl; F; Br; OMe; OH; CN; NO₂

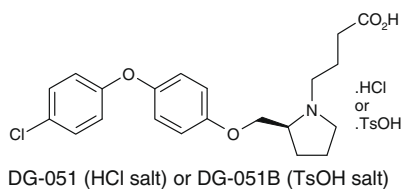
MIC = 12.5–2.5 µg/mL

A series of twenty-one quinoline derivatives have been synthesized and evaluated against *Mycobacterium tuberculosis*. Three compounds exhibited a significant activity (2.5 µg/mL), which can be compared with that of the first line drugs, ethambutol (3.12 µg/mL) and rifampicin (2.0 µg/mL).

Synthesis and structural assignment of two major metabolites of the LTA4H inhibitor DG-051

pp 6275–6279

Livia A. Enache*, Jun Zhang, David W. Sullins, Isaac Kennedy, Emmanuel Onua, David E. Zembower, Frank W. Muellner, Jasbir Singh, Alex S. Kiselyov



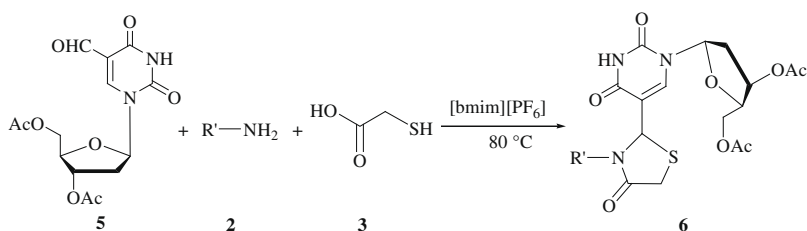
DG-051 (HCl salt) or DG-051B (TsOH salt)

The identification and synthesis of two CYP mediated metabolites of DG-051 are reported.

Ionic liquid mediated and promoted eco-friendly preparation of thiazolidinone and pyrimidine nucleoside-thiazolidinone hybrids and their antiparasitic activities

pp 6280-6283

Xinying Zhang, Xiaoyan Li, Dongfang Li, Guirong Qu^{*}, Jianji Wang, Philippe M. Loiseau, Xuesen Fan^{*}

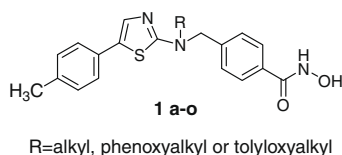


Novel pyrimidine nucleoside-thiazolidinone hybrids with antiparasitic activities were synthesized via an eco-friendly and efficient three-component reaction in [bmim][PF₆].

Novel N-hydroxybenzamide-based HDAC inhibitors with branched CAP group

pp 6284–6288

Hong Su, Liqin Yu, Angela Nebbioso, Vincenzo Carafa, Yadong Chen, Lucia Altucci*, Qidong You*



R=alkyl, phenoxyalkyl or tolyloxyalkyl

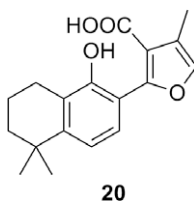
The discovery of a series of potent and selective *N*-hydroxybenzamide-based HDAC inhibitors is reported.



Antitumor agents 269. Non-aromatic ring-A neotanshinlactone analog, TNO, as a new class of potent antitumor agents

pp 6289–6292

Yizhou Dong, Qian Shi, Kyoko Nakagawa-Goto, Pei-Chi Wu, Kenneth F. Bastow, Susan L. Morris-Natschke, Kuo-Hsiung Lee *

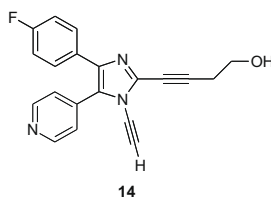


20

Synthesis and biological evaluation of p38 α kinase-targeting dialkynylimidazoles

pp 6293–6297

Jing Li, Tamer S. Kaoud, Christophe Laroche, Kevin N. Dalby, Sean M. Kerwin *

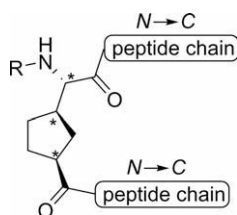


The dialkynylimidazole **14** is a potent (IC_{50} = 200 nM) and selective inhibitor that covalently modifies p38 α .

**Synthetic peptides containing a conserved sequence motif of the Id protein family modulate vascular smooth muscle cell phenotype**

pp 6298–6302

Sara Pellegrino, Nicola Ferri *, Noemi Colombo, Edoardo Cremona, Alberto Corsini, Roberto Fanelli, Maria Luisa Gelmi *, Chiara Cabrele *

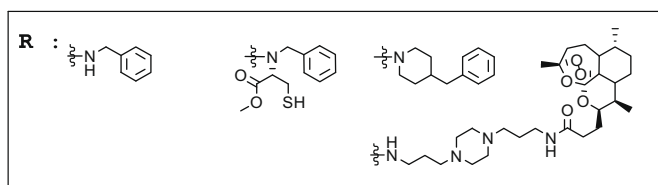
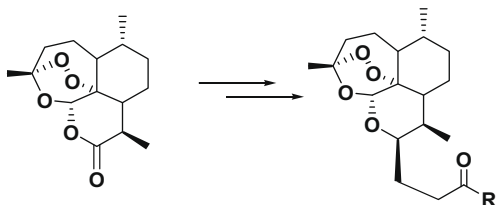


Peptide constructs decreasing the Id protein level and stimulating α -actin expression in SMCs in the low-micromolar range are reported.

**Synthesis and anticancer activity of novel amide derivatives of non-acetal deoxyartemisinin**

pp 6303–6306

Mankil Jung *, Namsu Park, Hyung-In Moon, Yongnam Lee, Won-Yoon Chung, Kwang-Kyun Park

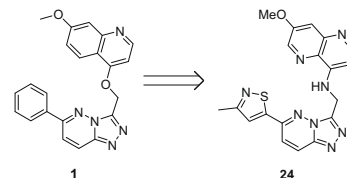


Novel amide derivatives of non-acetal deoxyartemisinin were synthesized. Some of the derivatives had potent in vitro anticancer activity and the deoxyartemisinin amide trimer had potent in vivo antiangiogenic activity.

Discovery and optimization of potent and selective triazolopyridazine series of c-Met inhibitors

pp 6307–6312

Alessandro A. Boezio *, Loren Berry, Brian K. Albrecht, David Bauer, Steven F. Bellon, Christiane Bode, April Chen, Deborah Choquette, Isabelle Dussault, Satoko Hirai, Paula Kaplan-Lefko, Jay F. Larrow, Min-Hwa Jasmine Lin, Julia Lohman, Michele H. Potashman, Karen Rex, Michael Santostefano, Kavita Shah, Roman Shimanovich, Stephanie K. Springer, Yohannes Teffera, Yajing Yang, Yihong Zhang, Jean-Christophe Harmange

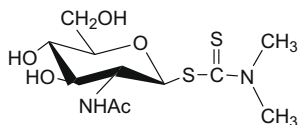


Deregulation of the receptor tyrosine kinase c-Met has been implicated in several human cancers and is an attractive target for small molecule drug discovery. We previously showed that O-linked triazolopyridazines can be potent inhibitors of c-Met. Herein, we report the discovery of a related series of N-linked triazolopyridazines which demonstrate nanomolar inhibition of c-Met kinase activity and display improved pharmacodynamic profiles. Specifically, the potent time-dependent inhibition of cytochrome P450 associated with the O-linked triazolopyridazines has been eliminated within this novel series of inhibitors. N-linked triazolopyridazine **24** exhibited favorable pharmacokinetics and displayed potent inhibition of HGF-mediated c-Met phosphorylation in a mouse liver PD model. Once-daily oral administration of **24** for 22 days showed significant tumor growth inhibition in an NIH-3T3/TPR-Met xenograft mouse efficacy model.

Synthesis of new sugar derivatives and evaluation of their antibacterial activities against *Mycobacterium tuberculosis*

pp 6313–6316

Yasuhiro Horita, Takemasa Takii ^{*}, Taku Chiba, Ryuji Kuroishi, Yasuhiro Maeda, Yukihisa Kurono, Emi Inagaki, Kenji Nishimura, Yoshifumi Yamamoto, Chiyoji Abe, Masami Mori, Kikuo Onozaki



4 MIC=1.56~25 µg/ml

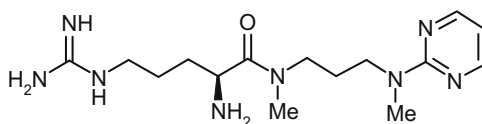
The anti-mycobacterial properties of sugar derivatives synthesized and evaluated for antibacterial activity against *Mycobacterium tuberculosis* (MTB), especially multi-drug resistant (MDR) MTB **4** (MIC = 1.56–25 µg/ml) is reported.



Arginine–pyrimidine conjugates with therapeutic and prophylactic activity in lethal bacterial infections

pp 6317–6318

Dieter Haebich ^{*}, Hein-Peter Kroll, Hans-Georg Lerchen

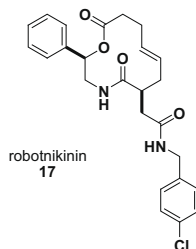


Arginine–pyrimidine conjugates represent a novel class of compounds that exhibits therapeutic and prophylactic activity in lethal infections by Gram-positive and Gram-negative bacteria without showing antibacterial activity in vitro.

Syntheses of aminoalcohol-derived macrocycles leading to a small-molecule binder to and inhibitor of Sonic Hedgehog

pp 6319–6325

Lee F. Peng ^{*}, Benjamin Z. Stanton, Nicole Maloof, Xiang Wang, Stuart L. Schreiber



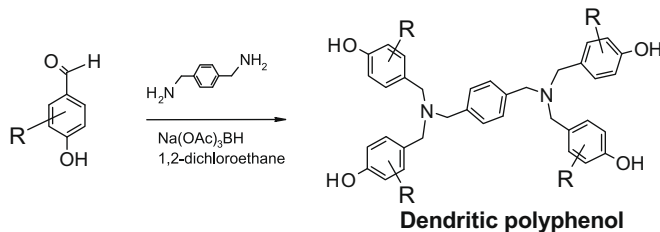
We report the synthesis and biological activity of a library of aminoalcohol-derived macrocycles from which robotnikinin (**17**), a binder and inhibitor of Sonic Hedgehog, was derived.



Synthesis and antioxidant properties of dendritic polyphenols

pp 6326–6330

Choon Young Lee ^{*}, Ajit Sharma, Jae Eun Cheong, Julie L. Nelson

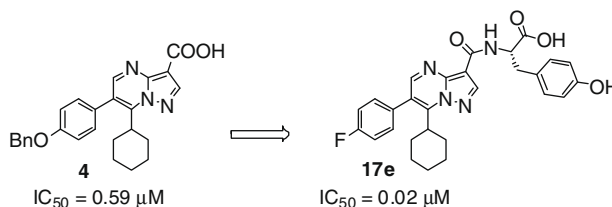


Three dendritic phenol-based antioxidants were synthesized. The dendrimers showed strong DPPH radical scavenging activity and protective effect against free radical damage of LDL, linoleic acid, and DNA.

Pyrazolo[1,5-a]pyrimidine-based inhibitors of HCV polymerase

pp 6331–6336

Janeta Popovici-Muller *, Gerald W. Shipps Jr., Kristin E. Rosner, Yongqi Deng, Tong Wang, Patrick J. Curran, Meredith A. Brown, M. Arshad Siddiqui, Alan B. Cooper, José Duca, Michael Cable, Viyyoor Girijavallabhan

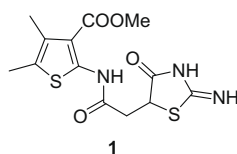


Synthesis and optimization of novel pyrazolo[1,5-a]pyrimidine HCV polymerase inhibitors are described.

Identification of iminooxothiazolidines as secreted frizzled related protein-1 inhibitors

pp 6337–6339

Mengxiao Shi *, Barbara Stauffer, Ramesh Bhat, Julia Billiard, Helga Ponce-de-Leon, Laura Seestaller-Wehr, Shoichi Fukayama, Annamarie Mangine, Robert Moran, Girija Krishnamurthy, Peter Bodine, Ariamala Gopalsamy

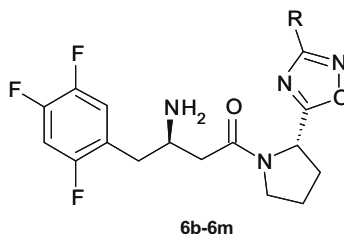


Identification of iminooxothiazolidines as secreted frizzled related protein-1 inhibitors and the SAR requirements are reported.

The design of potent and selective inhibitors of DPP-4: Optimization of ADME properties by amide replacements

pp 6340–6345

Sonja Nordhoff *, Stephan Bulat, Silvia Cerezo-Gálvez, Oliver Hill, Barbara Hoffmann-Enger, Meritxell López-Canet, Claudia Rosenbaum, Christian Rummey, Meinolf Thiemann, Victor G. Matassa, Paul J. Edwards, Achim Feurer

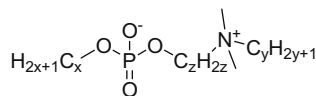


For a series of β -homophenylalanine based inhibitors of dipeptidyl peptidase IV ADME properties were improved by the incorporation of amide replacements. These efforts led to a novel series of potent and selective inhibitors of DPP-4 that exhibit an attractive pharmacokinetic profile and show excellent efficacy in an animal model of diabetes.

**Synthesis and biological activity of dialkylphosphocholines**

pp 6346–6349

Miloš Lukáč *, Martin Mrva, Eva Fischer-Fodor, Ivan Lacko, Marián Bukovský, Natalia Miklášová, František Ondriska, Ferdinand Devínsky

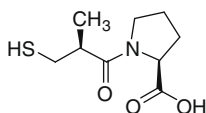


The synthesis and antiprotozoal, antimycotic, and cytotoxic activity of dialkylphosphocholines are reported.

Inhibitors of bacterial *N*-succinyl-L,L-diaminopimelic acid desuccinylase (DapE) and demonstration of in vitro antimicrobial activity

pp 6350–6352

Danuta Gillner, Nicola Armoush, Richard C. Holz, Daniel P. Becker *



IC₅₀ = 3.3 μM vs. DapE
K_i = 1.82 ± 0.09 μM (competitive)

A screen biased toward compounds containing zinc-binding groups (ZBG's) delivered a number of micromolar inhibitors of DapE from *Haemophilus influenzae*, including L-captopril (IC₅₀ = 3.3 μM, K_i = 1.8 μM). In vitro antimicrobial activity was demonstrated for L-captopril against *Escherichia coli*.

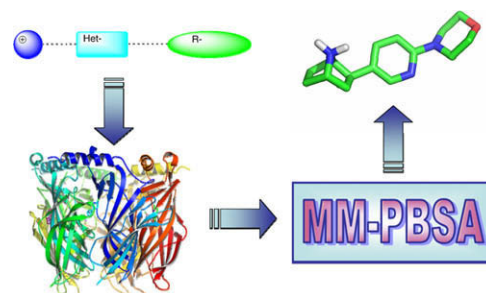


Design of novel α7-subtype-preferring nicotinic acetylcholine receptor agonists: Application of docking and MM-PBSA computational approaches, synthetic and pharmacological studies

pp 6353–6357

Giovanni Grazioso *, Diego Yuri Pomè, Carlo Matera, Fabio Frigerio, Luca Pucci, Cecilia Gotti, Clelia Dallanocce, Marco De Amici

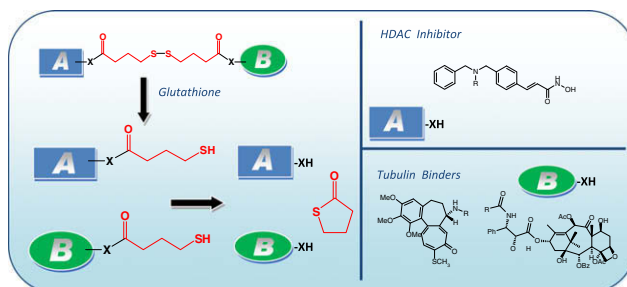
We docked about 150 compounds in a model of the α7 neuronal nicotinic receptor, and applied a validated, simplified MM-PBSA approach to estimate their relative binding free energy values. Five structural analogues were selected, synthesized, and tested for binding affinity at α7 and α4β2 subtypes.



Histone deacetylase and microtubules as targets for the synthesis of releasable conjugate compounds

pp 6358–6363

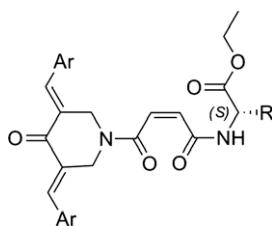
Daniele Passarella *, Daniela Comi, Andrea Vanossi, Gianfranco Paganini, Francesco Colombo, Luca Ferrante, Valentina Zuco, Bruno Danieli, Franco Zunino *



Design, synthesis and bioevaluation of novel maleamic amino acid ester conjugates of 3,5-bisarylmethylene-4-piperidones as cytostatic agents

pp 6364–6367

Dani Youssef, Elizabeth Potter, Mamta Jha, Erik De Clercq, Jan Balzarini, James P. Stables, Amitabh Jha *

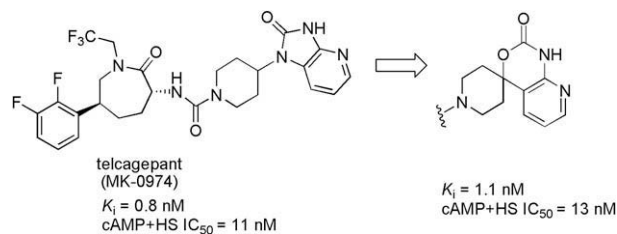


A novel series of maleamic amino acid ester conjugates of 3,5-bisarylmethylene-4-piperidones were prepared and bioevaluated. All compounds were found to have greater potency than the reference drug melphalan, and several were found to potently inhibit topoisomerase IIα and showed cytostatic activity in the nanomolar range.

Optimization of azepanone calcitonin gene-related peptide (CGRP) receptor antagonists: Development of novel spiropiperidines

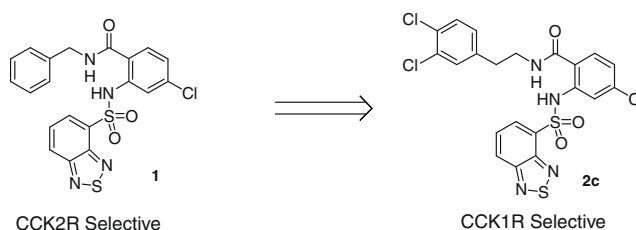
pp 6368–6372

Christopher S. Burgey^{*}, Craig M. Potteiger, James Z. Deng, Scott D. Mosser, Christopher A. Salvatore, Sean Yu, Shane Roller, Stefanie A. Kane, Joseph P. Vacca, Theresa M. Williams

**Anthranilic sulfonamide CCK1/CCK2 dual receptor antagonists I: Discovery of CCK1R selectivity in a previously CCK2R-selective lead series**

pp 6373–6375

Marna Pippel, Brett D. Allison, Victor K. Phuong, Lina Li, Magda F. Morton, Clodagh Prendergast, Xiaodong Wu, Nigel P. Shankley, Michael H. Rabinowitz^{*}

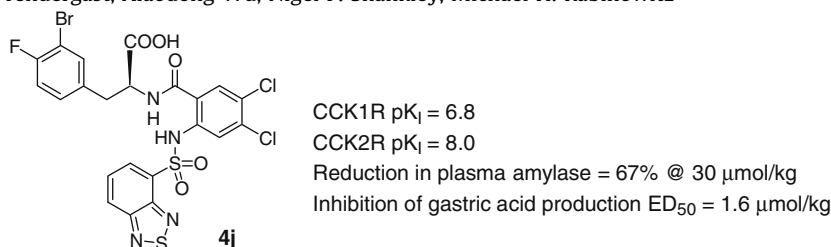


Cholecystokinin receptor subtype selectivity is shown to be reversed in the anthranilic sulfonamide series of antagonists via specific manipulation of the amide side chain.

Anthranilic sulfonamide CCK1/CCK2 dual receptor antagonists II: Tuning of receptor selectivity and in vivo efficacy

pp 6376–6378

Marna Pippel, Kristen Boyce, Hariharan Venkatesan, Victor K. Phuong, Wen Yan, Terrance D. Barrett, Guy Lagaud, Lina Li, Magda F. Morton, Clodagh Prendergast, Xiaodong Wu, Nigel P. Shankley, Michael H. Rabinowitz^{*}

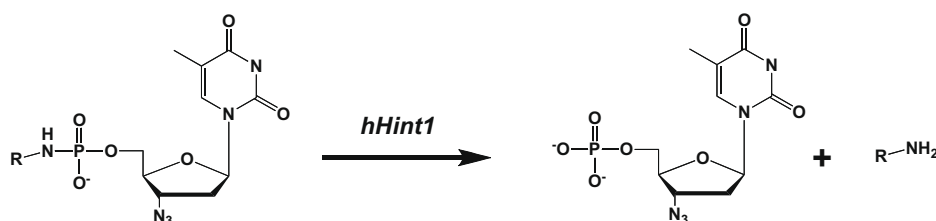


Optimization of affinity for both CCK1 and CCK2 receptors results in compounds that both inhibit pancreatic enzyme secretion and inhibit the production of gastric acid in animal models.

Identification of the amino acid-AZT-phosphoramidase by affinity T7 phage display selection

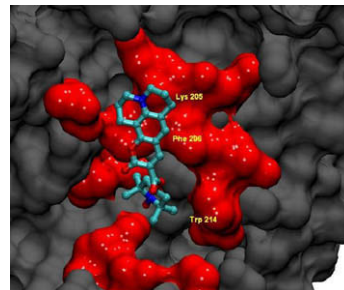
pp 6379–6381

Jilin Cheng, Xin Zhou, Tsui-Fen Chou, Brahma Ghosh, Baoling Liu, Carston R. Wagner^{*}



Antioxidant reactivity toward nitroxide probes anchored into human serum albumin. A new model for studying antioxidant repairing capacity of protein radicals

pp 6382–6385

Alexis Aspée^{*}, Alejandra Orrego, Emilio Alarcón, Camilo López-Alarcón, Horacio Poblete, Danilo González-Nilo

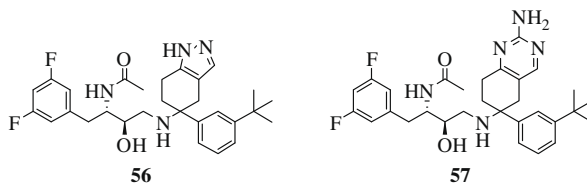
Kinetic rate constant values for the nitroxide reduction bound to Human serum albumin reveal influence of environment and accessibility factors on the antioxidant ability to repair protein free radicals.



Design and synthesis of cell potent BACE-1 inhibitors: Structure–activity relationship of P1' substituents

pp 6386–6391

Jennifer M. Sealy, Anh P. Truong, Luke Tso, Gary D. Probst^{*}, Jose Aquino, Roy K. Hom^{*}, Barbara M. Jagodzinska, Darren Dressen, David W. G. Wone, Louis Brogley, Varghese John, Jay S. Tung, Michael A. Pleiss, John A. Tucker, Andrei W. Konradi, Michael S. Dappen, Gergely Toth, Hu Pan, Lany Ruslim, Jim Miller, Michael P. Bova, Sukanto Sinha, Kevin P. Quinn, John-Michael Sauer

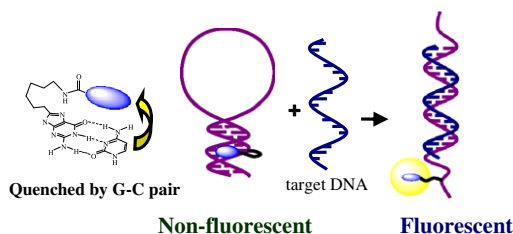


Using structure-guided design, hydroxyethylamine BACE-1 inhibitors were optimized to nanomolar A β cellular inhibition with selectivity against cathepsin-D. X-ray crystallography illuminated the S1' residues critical to this effort, which culminated in compounds **56** and **57** that exhibited potency and selectivity but poor permeability and high P-gp efflux.



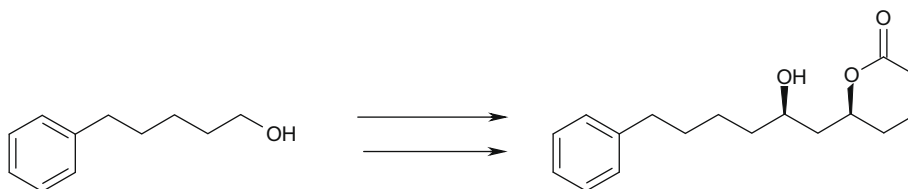
Pyrene-labeled deoxyguanosine as a fluorescence sensor to discriminate single and double stranded DNA structures: Design of ends free molecular beacons

pp 6392–6395

Katsuhiko Matsumoto, Yuta Shinohara, Subhendu S. Bag, Yoshiki Takeuchi, Takashi Morii, Yoshio Saito^{*}, Isao Saito^{*}

Stereoselective total synthesis of a potent natural antifungal compound (6S)-5,6-dihydro-6-[(2R)-2-hydroxy-6-phenyl hexyl]-2H-pyran-2-one

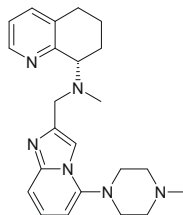
pp 6396–6398

Biswanath Das^{*}, Keetha Laxminarayana, Martha Krishnaiah, Duddukuri Nandan Kumar

Imidazopyridine-5,6,7,8-tetrahydro-8-quinolinamine derivatives with potent activity against HIV-1

pp 6399–6403

Kristjan S. Gudmundsson *, Sharon D. Boggs, John G. Catalano, Angilique Svolto, Andrew Spaltenstein, Michael Thomson, Pat Wheelan, Stephen Jenkinson

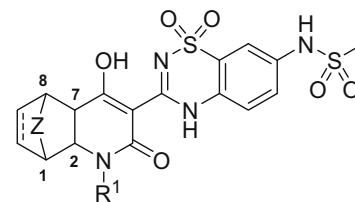


Synthesis of several novel imidazopyridine-5,6,7,8-tetrahydro-8-quinolinamine derivatives with potent activity against HIV-1 are described.

Discovery of tricyclic 5,6-dihydro-1H-pyridin-2-ones as novel, potent, and orally bioavailable inhibitors of HCV NS5B polymerase

pp 6404–6412

Frank Ruebsam *, Douglas E. Murphy, Chinh V. Tran, Lian-Sheng Li, Jingjing Zhao, Peter S. Dragovich, Helen M. McGuire, Alan X. Xiang, Zhongxiang Sun, Benjamin K. Ayida, Julie K. Blazel, Sun Hee Kim, Yuefen Zhou, Qing Han, Charles R. Kissinger, Stephen E. Webber, Richard E. Showalter, Amit M. Shah, Mei Tsan, Rupal A. Patel, Peggy A. Thompson, Laurie A. LeBrun, Huiying J. Hou, Ruhi Kamran, Maria V. Sergeeva, Darian M. Bartkowski, Thomas G. Nolan, Daniel A. Norris, Julia Khandurina, Jennifer Brooks, Ellen Okamoto, Leo Kirkovsky

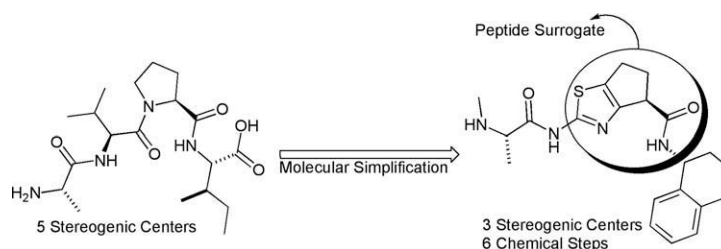


Z = CH₂, CH₂CH₂, O

Design and synthesis of a simplified inhibitor for XIAP-BIR3 domain

pp 6413–6418

Fernando R. Pinacho Crisóstomo, Yongmei Feng, Xuejun Zhu, Kate Welsh, Jing An, John C. Reed, Ziwei Huang *

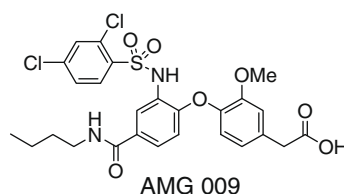


Based on tetrapeptide AVPI we were able to design and synthesize a new simplified scaffold to inhibit the BIR3 domain of the XIAP protein at low micromolar range.

Discovery and optimization of CRTH2 and DP dual antagonists

pp 6419–6423

Jiwen Liu *, Zice Fu, Yingcai Wang, Mike Schmitt, Alan Huang, Derek Marshall, George Tonn, Lisa Seitz, Tim Sullivan, H. Lucy Tang, Tassie Collins, Julio Medina

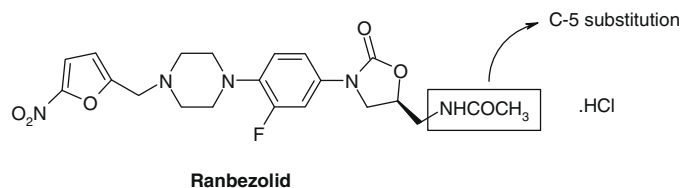


AMG 009

A series of phenylacetic acid derivatives was discovered as CRTH2 antagonists. Modification of the series led to compounds that are also antagonists of DP. Since activation of CRTH2 and DP are believed to play key roles in mediating responses of asthma and other immune diseases, this series was optimized to increase the dual antagonistic activities and improve pharmacokinetic properties. These efforts led to selection of AMG 009 as a clinical candidate.

Synthesis and biological activity of novel oxazolidinones

pp 6424–6428

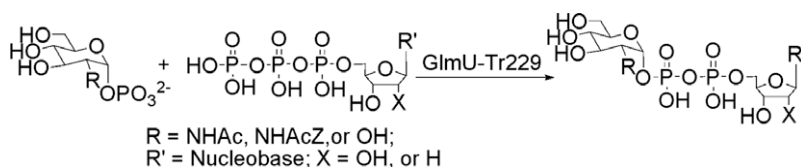
Biswajit Das^{*}, A. V. S. Rajarao, Sonali Rudra, Ajay Yadav, Abhijit Ray, Manisha Pandya, Ashok Rattan, Anita Mehta

A number of 5-substituted derivatives of Ranbezolid, a novel oxazolidinone were synthesized and their antibacterial activity reported.



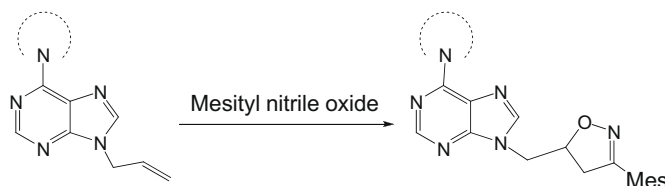
Systematic study on the broad nucleotide triphosphate specificity of the pyrophosphorylase domain of the *N*-acetylglucosamine-1-phosphate uridylyltransferase from *Escherichia coli* K12

pp 6429–6432

Junqiang Fang, Wanyi Guan, Li Cai, Guofeng Gu^{*}, Xianwei Liu^{*}, Peng George Wang

Synthesis of modified homo-*N*-nucleosides from the reactions of mesityl nitrile oxide with 9-allylpurines and their influence on lipid peroxidation and thrombin inhibition

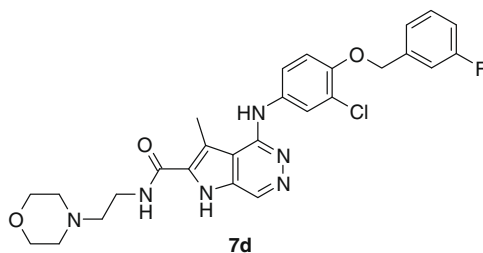
pp 6433–6436

Andreas Thalassitis, Dimitra J. Hadjipavlou-Litina^{*}, Konstantinos E. Litinas^{*}, Panagiotis Miltiadou

The synthesized compounds act as lipid peroxidation inhibitors and potent thrombin inhibitors.

Synthesis and biological evaluation of pyrrolopyridazine derivatives as novel HER-2 tyrosine kinase inhibitors

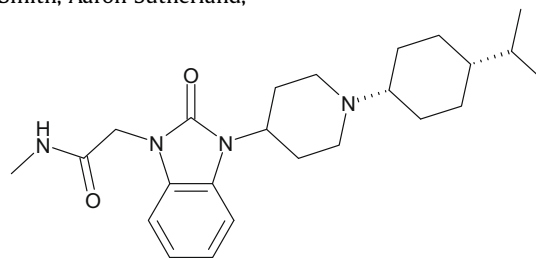
pp 6437–6440

Tang Peng Cho^{*}, Feng Jun, Huang Li, Xu Zhe, Cheng Ling, Zhang Xu, Zhang Lei, Hu BingA series of novel pyrrolopyridazine derivatives have been discovered to be HER-2 inhibitors. These compounds selectively inhibited HER-2 kinase activity at low nanomolar concentrations. Compound **7d** was identified as a potent HER-2 inhibitor with an IC₅₀ of 4 nM.

Rapid access towards follow-up NOP receptor agonists using a knowledge based approach

pp 6441–6446

Ronald Palin ^{*}, John K. Clark, Louise Evans, Helen Feilden, Dan Fletcher, Niall M. Hamilton, Andrea K. Houghton, Philip S. Jones, Duncan McArthur, Brian Montgomery, Paul D. Ratcliffe, Alasdair R. C. Smith, Aaron Sutherland, Mark A. Weston, Grant Wishart

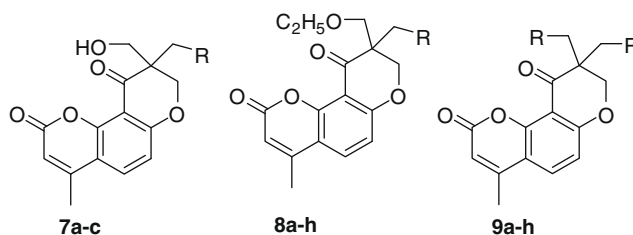


A knowledge based approach was applied to explore novel NOP receptor agonists with simplified hydrophobes. Compound **51** was identified as a high affinity, potent NOP receptor agonist.

51**Pyranocoumarins: A new class of anti-hyperglycemic and anti-dyslipidemic agents**

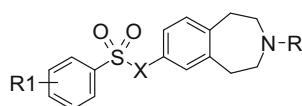
pp 6447–6451

Atul Kumar ^{*}, Ram Awatar Maurya, Siddharth Sharma, Pervez Ahmad, A. B. Singh, Gitika Bhatia, Arvind K. Srivastava

**The discovery and optimisation of benzazepine sulfonamide and sulfones as potent agonists of the motilin receptor**

pp 6452–6458

James M. Bailey ^{*}, Jackie S. Scott ^{*}, Jonathan B. Basilla, Victoria J. Bolton, Izzy Boyfield, David G. Evans, Etienne Fleury, Tom D. Heightman, Emma M. Jarvie, Kirk Lawless, Kim L. Matthews, Fiona McKay, Hindy Mok, Alison Muir, Barry S. Orlek, Gareth J. Sanger, Geoffrey Stemp, Alexander J. Stevens, Mervyn Thompson, John Ward, Kalindi Vaidya, Susan M. Westaway

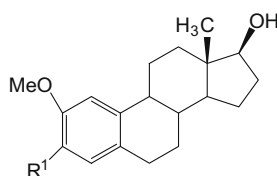


Novel benzazepine sulfonamides and sulfones are potent, selective motilin receptor agonists. Hit identification and lead optimisation of this new peptide GPCR ligand series is described.

Synthesis and antitumor activities of 3-modified 2-methoxyestradiol analogs

pp 6459–6462

Lita S. Suwandi, Gregory E. Agoston, Jamshed H. Shah, Arthur D. Hanson, Xiaoguo H. Zhan, Theresa M. LaVallee, Anthony M. Treston ^{*}

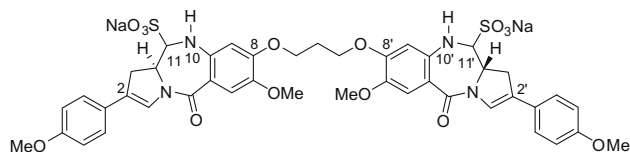


A lead-generation series of analogs of 2-methoxyestradiol modified at the 3-position were designed, synthesized and evaluated for antiproliferative, antiangiogenic, and estrogenic properties.

Synthesis of a novel C2/C2'-aryl-substituted pyrrolo[2,1-c][1,4]benzodiazepine dimer prodrug with improved water solubility and reduced DNA reaction rate

pp 6463–6466

Philip W. Howard ^{*}, Zhizhi Chen, Stephen J. Gregson, Luke A. Masterson, Arnaud C. Tiberghien, Nectaroula Cooper, Min Fang, Marissa J. Coffils, Sarah Klee, John A. Hartley, David E. Thurston ^{*}

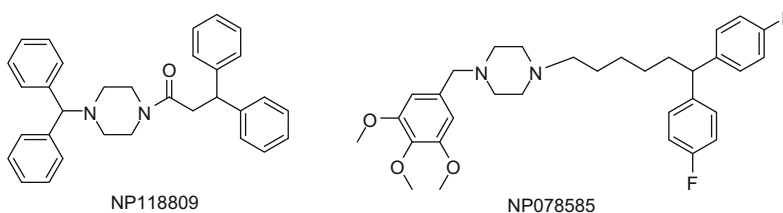


Novel C11/C11'-bisulfite prodrug (SG2285, **17**) of the N10–C11/N10'–C11' bis-imine PBD dimer (**16**) with enhanced water solubility and a slower rate of reaction with DNA.

Scaffold-based design and synthesis of potent N-type calcium channel blockers

pp 6467–6472

Gerald W. Zamponi, Zhong-Ping Feng, Lingyun Zhang, Hossein Pajouhesh, Yanbing Ding, Francesco Belardetti, Hassan Pajouhesh, David Dolphin, Lester A. Mitscher, Terrance P. Snutch ^{*}

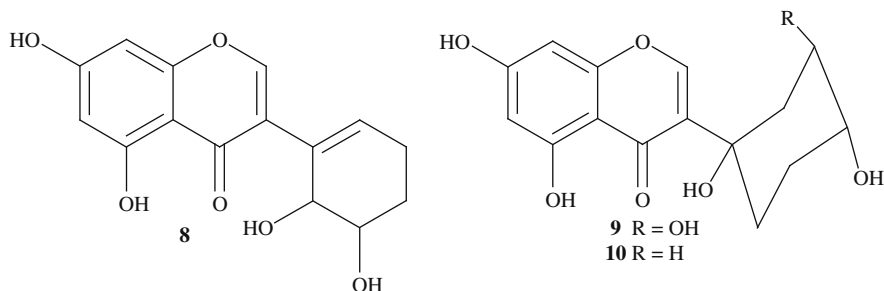


Discovery of **NP118809** and **NP078585** as N-type selective calcium channel blockers resulting from the scaffold optimization of flunarizine and lomerizine are reported.

Isoflavones with unusually modified B-rings and their evaluation as antiproliferative agents

pp 6473–6476

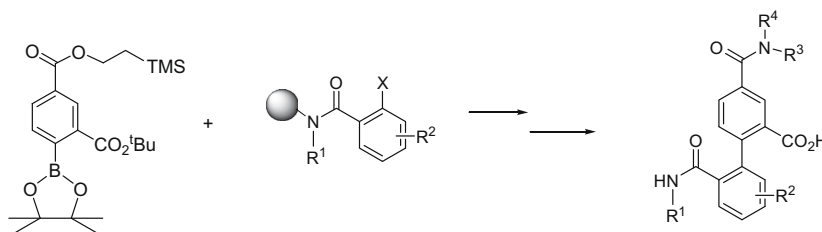
B. Le S. Tchize Ndejoung, I. Sattler, H.-M. Dahse, E. Kothe, C. Hertweck ^{*}



Solid-phase synthesis of a library based on biphenyl-containing trypsin-like serine protease inhibitors

pp 6477–6480

Shuhao Shi ^{*}, Shirong Zhu, Samuel W. Gerritz, Bogumila Rachwal, Zheming Ruan, Robert Hutchins, Ramesh Kakarla, Michael J. Sofia, James Sutton, Daniel Cheney




A novel and efficient method for synthesizing a highly functionalized aryl boronic acid reagent in large scale was developed. A huge biphenyl scaffold library for trypsin-like serine protease inhibitor by solid-phase synthesis is described.



OTHER CONTENTS**Corrigendum****p 6481**

*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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