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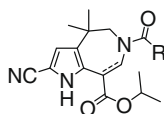
Contents

ARTICLES

Pyrrole[2,3-*d*]azepino compounds as agonists of the farnesoid X receptor (FXR)

pp 5289–5292

John F. Mehlmann, Matthew L. Crawley^{*}, Joseph T. Lundquist IV, Ray J. Unwalla, Douglas C. Harnish, Mark J. Evans, Callain Y. Kim, Jay E. Wrobel, Paige E. Mahaney



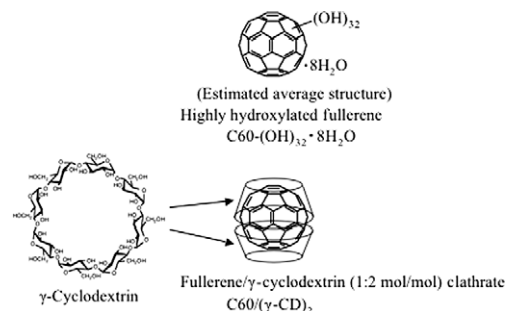
The rational design and discovery of a new series of pyrrole[2,3-*d*]azepino FXR agonists with aqueous solubility and improved pharmaceutical properties is reported.

Highly hydroxylated or γ -cyclodextrin-bicapped water-soluble derivative of fullerene: The antioxidant ability assessed by electron spin resonance method and β -carotene bleaching assay

pp 5293–5296

Shinya Kato, Hisae Aoshima, Yasukazu Saitoh, Nobuhiko Miwa^{*}

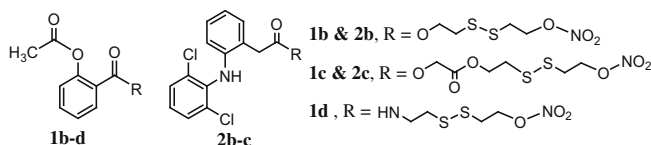
Antioxidant ability of the water-soluble derivative of fullerene-C60 was assessed by ESR and β -carotene bleaching assay, showing that C60-(OH)₃₂·8H₂O and C60/(γ -CD)₂ scavenged OH, and have a distinct antioxidative activity.



NO-NSAIDs: Gastric-sparing nitric oxide-releasable prodrugs of non-steroidal anti-inflammatory drugs

pp 5297–5301

Kumar V. S. Nemmani, Sunil V. Mali, Namdev Borhade, Asif R. Pathan, Manoj Karwa, Venu Pamidiboina, S. P. Senthilkumar, Machhindra Gund, Arun K. Jain, Naveen K. Mangu, Nauzer P. Dubash, Dattatraya C. Desai, Somesh Sharma, Apparao Satyam^{*}



Gastric-sparing NO-NSAIDs were designed, synthesized and evaluated. Among those evaluated, NO-Diclofenac (**2b**) has shown excellent bioavailability, anti-inflammatory activity, NO-releasing profile and gastric-sparing properties.

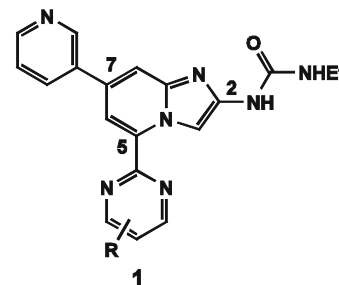


5-(2-Pyrimidinyl)-imidazo[1,2-*a*]pyridines are antibacterial agents targeting the ATPase domains of DNA gyrase and topoisomerase IV

pp 5302–5306

Jeremy T. Starr^{*}, Richard J. Sciotti, Debra L. Hanna, Michael D. Huband, Lisa M. Mullins, Hongliang Cai, Jeffrey W. Gage, Mandy Lockard, Mark R. Rauckhorst, Robert M. Owen, Manjinder S. Lall, Mark Tomilo, Huifen Chen, Sandra P. McCurdy, Michael R. Barbachyn

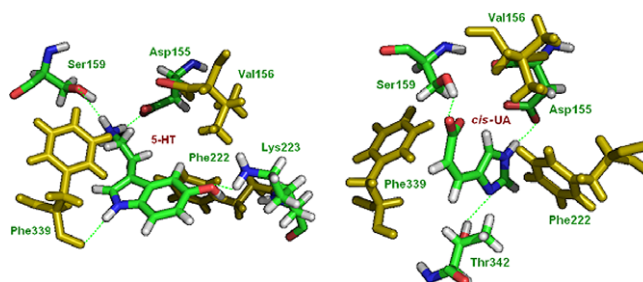
Dual inhibitors of bacterial *gyrB* and *parE* based on a 5-(2-pyrimidinyl)-imidazo[1,2-*a*]pyridine template exhibited MICs ($\mu\text{g/mL}$) of 0.06–64 (*Sau*), 0.25–64 (*MRSA*), 0.06–64 (*Spy*), 0.06–64 (*Spn*), and 0.03–64 (*FQR Spn*). Selected examples were efficacious in mouse sepsis and lung infection models at <50 mg/kg (PO dosing).



Molecular basis for *cis*-urocanic acid as a 5-HT_{2A} receptor agonist

pp 5307–5309

Liang Shen, Hong-Fang Ji^{*}

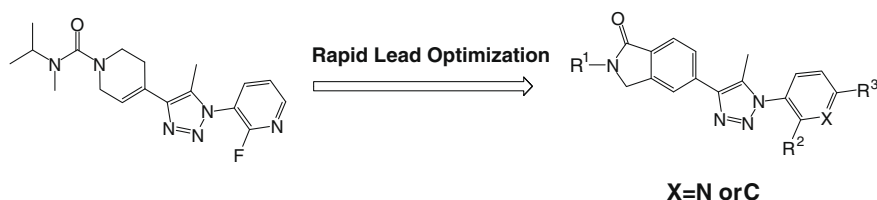


The similar binding modes and affinities of *cis*-UA and 5-hydroxytryptamine to 5-HT_{2A} receptor may account for *cis*-UA being a 5-HT_{2A} receptor agonist.

Discovery and biological profile of isoindolinone derivatives as novel metabotropic glutamate receptor 1 antagonists: A potential treatment for psychotic disorders

pp 5310–5313

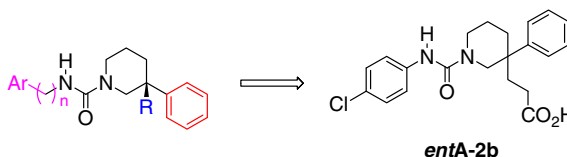
Satoru Ito^{*}, Yukari Hirata, Yasushi Nagatomi, Atsushi Satoh, Gentaro Suzuki, Toshifumi Kimura, Akio Satow, Shunsuke Maehara, Hirohiko Hikichi, Mikiko Hata, Hisashi Ohta, Hiroshi Kawamoto



Discovery of 3,3-disubstituted piperidine-derived trisubstituted ureas as highly potent soluble epoxide hydrolase inhibitors

pp 5314–5320

Hong C. Shen^{*}, Fa-Xiang Ding, Qiaolin Deng, Suoyu Xu, Hsuan-shen Chen, Xinchun Tong, Vincent Tong, Xiaoping Zhang, Yuli Chen, Gaochao Zhou, Lee-Yuh Pai, Magdalena Alonso-Galicia, Bei Zhang, Sophie Roy, James R. Tata, Joel P. Berger, Steven L. Colletti



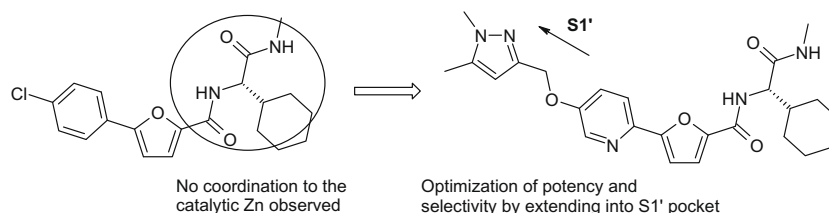
3,3-Disubstituted piperidine-derived trisubstituted urea **entA-2b** was discovered as a highly potent and selective soluble epoxide hydrolase (sEH) inhibitor. Despite the good compound oral exposure, excellent sEH inhibition in whole blood, and remarkable selectivity, compound **entA-2b** failed to lower blood pressure acutely in spontaneously hypertensive rats (SHRs). This observation further challenges the premise that sEH inhibition can provide a viable approach to the treatment of hypertensive patients.



Improving potency and selectivity of a new class of non-Zn-chelating MMP-13 inhibitors

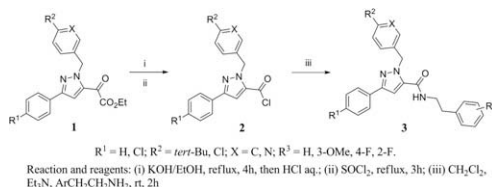
pp 5321–5324

Alexander Heim-Riether^{*}, Steven J. Taylor, Shuang Liang, Donghong Amy Gao, Zhaoming Xiong, E. Michael August, Brandon K. Collins, Bennett T. Farmer II, Kathleen Haverty, Melissa Hill-Drzewi, Hans-Dieter Junker, S. Mariana Margarit, Neil Moss, Thomas Neumann, John R. Proudfoot, Lana Smith Keenan, Renate Sekul, Qiang Zhang, Jun Li, Neil A. Farrow

**Synthesis of novel pyrazole carboxamide derivatives and discovery of modulators for apoptosis or autophagy in A549 lung cancer cells**

pp 5325–5328

Xiao-Ling Ding, Hai-Yan Zhang, Lei Qi, Bao-Xiang Zhao^{*}, Song Lian, Hong-Shui Lv, Jun-Ying Miao^{*}

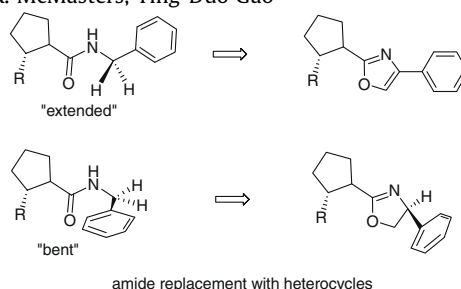


A series of novel 3-aryl-1-arylmethyl-1H-pyrazole-5-carboxamide derivatives **3a–l**, were synthesized by the reaction of 3-aryl-1-arylmethyl-1H-pyrazole-5-carboxylic acid with substituted amine in excellent yields. The compounds **3e–h** could suppress A549 lung cancer cell growth. More interestingly, compounds **3e** and **3f** might inhibit the A549 cell growth by inducing apoptosis; whereas compounds **3g** and **3h** with fluorine group might inhibit the A549 cell growth by inducing autophagy.

**Discovery of a novel class of isoxazoline voltage gated sodium channel blockers**

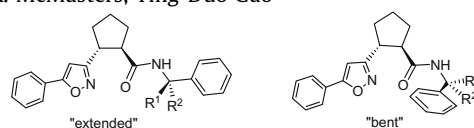
pp 5329–5333

Pengcheng P. Shao^{*}, Feng Ye, Ann E. Weber, Xiaohua Li, Kathryn A. Lyons, William H. Parsons, Maria L. Garcia, Birgit T. Priest, McHardy M. Smith, John P. Felix, Brande S. Williams, Gregory J. Kaczorowski, Erin McGowan, Catherine Abbadie, William J. Martin, Daniel R. McMasters, Ying-Duo Gao

**Discovery of isoxazole voltage gated sodium channel blockers for treatment of chronic pain**

pp 5334–5338

Pengcheng P. Shao^{*}, Feng Ye, Ann E. Weber, Xiaohua Li, Kathryn A. Lyons, William H. Parsons, Maria L. Garcia, Birgit T. Priest, McHardy M. Smith, John P. Felix, Brande S. Williams, Gregory J. Kaczorowski, Erin McGowan, Catherine Abbadie, William J. Martin, Daniel R. McMasters, Ying-Duo Gao

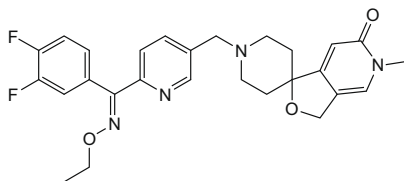


	Energy difference between the two conformation (kcal/mol)	Nav1.7 potency IC_{50} (μM)
$R^1, R^2: \text{H}$	0.07 kcal/mol favor "bent"	$> 1 \mu\text{M}$
$R^1, R^2: -\text{CH}_2\text{CH}_2\text{CH}_2-$	3.97 kcal/mol favor "bent"	0.12 μM

Discovery of novel diarylketoxime derivatives as selective and orally active melanin-concentrating hormone 1 receptor antagonists

pp 5339–5345

Takao Suzuki ^{*}, Minoru Kameda, Makoto Ando, Hiroshi Miyazoe, Etsuko Sekino, Satoru Ito, Kouta Masutani, Kaori Kamiyo, Akihiro Takezawa, Minoru Moriya, Masahiko Ito, Junko Ito, Kazuho Nakase, Hiroko Matsushita, Akane Ishihara, Norihiro Takenaga, Shigeru Tokita, Akio Kanatani, Nagaaki Sato ^{*}, Takehiro Fukami



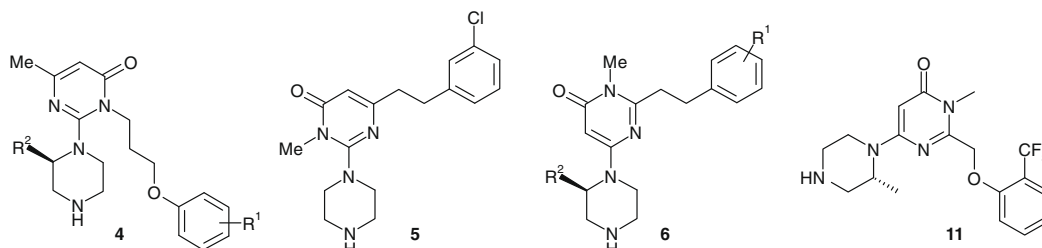
4b: hMCH-1R (IC_{50}) = 6.8 nM

The identification of selective and orally active MCH-1R antagonist **4b** is reported.

Design and synthesis of piperazinylpyrimidinones as novel selective 5-HT_{2C} agonists

pp 5346–5350

Mark D. Andrews ^{*}, Martin P. Green ^{*}, Charlotte M. N. Allerton, David V. Batchelor, Julian Blagg, Alan D. Brown, David W. Gordon, Gordon McMurray, Daniel J. Millns, Carly L. Nichols, Lesa Watson

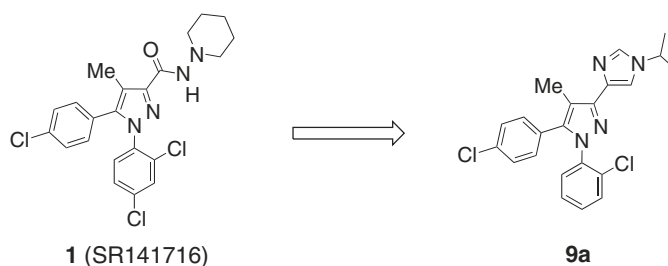


The design, synthesis and biological activity of several novel series of piperazinyl pyrimidinones is described. Compound **11** showed efficacy in a pre-clinical model of urethral function which highlights potential efficacy in stress urinary incontinence.

Bioisosteric replacement of the hydrazide pharmacophore of the cannabinoid-1 receptor antagonist SR141716A. Part I: Potent, orally-active 1,4-disubstituted imidazoles

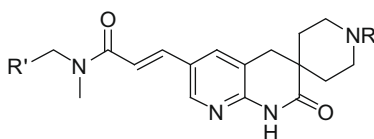
pp 5351–5354

Robert L. Dow ^{*}, John R. Hadcock, Dennis O. Scott, Steven R. Schneider, Ernest S. Paight, Philip A. Iredale, Philip A. Carpino, David A. Griffith, Marlys Hammond, Paul DaSilva-Jardine


Spiro-naphthyridinone piperidines as inhibitors of *S. aureus* and *E. coli* enoyl-ACP reductase (FabI)

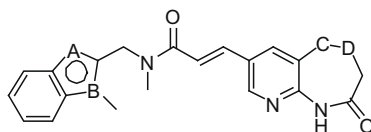
pp 5355–5358

Peter B. Sampson ^{*}, Christine Picard, Sean Handerson, Teresa E. McGrath, Megan Domagala, Andrew Leeson, Vladimir Romanov, Donald E. Awrey, Dhushy Thambipillai, Elias Bardouniotis, Nachum Kaplan, Judd M. Berman, Henry W. Pauls



2,3,4,5-Tetrahydro-1H-pyrido[2,3-*b* and *e*][1,4]diazepines as inhibitors of the bacterial enoyl ACP reductase, FabI pp 5359–5362

Jailall Ramnauth ^{*}, Mathew D. Surman, Peter B. Sampson, Bryan Forrest, Jeff Wilson, Emily Freeman, David D. Manning, Fernando Martin, Andras Toro, Megan Domagala, Donald E. Awrey, Elias Bardouniotis, Nachum Kaplan, Judd Berman, Henry W. Pauls ^{*}

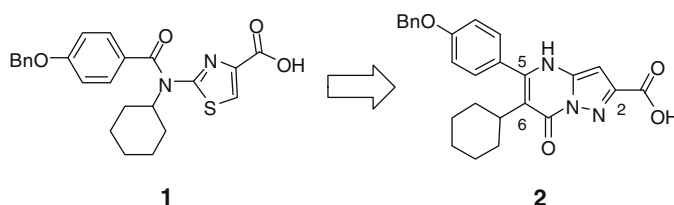


11d, A = O, B = C, C = NH, D = CH₂
16c, A = CH, B = N, C = CH₂, D = NH

Using a structure guided approach, naphthyridinone FabI inhibitors were expanded to novel 2,3,4,5-tetrahydro-1H-pyrido[2,3-*b* and *e*][1,4]diazepines (e.g., **11d**; FabI IC₅₀ = 11 nM). Diazepinone **16c** is shown to be efficacious in a mouse infection model.

Discovery of 4H-pyrazolo[1,5-*a*]pyrimidin-7-ones as potent inhibitors of hepatitis C virus polymerase pp 5363–5367

Yongqi Deng ^{*}, Gerald W. Shipps Jr., Tong Wang, Janeta Popovici-Muller, Kristin E. Rosner, M. Arshad Siddiqui, Jose Duca, Alan B. Cooper, Michael Cable

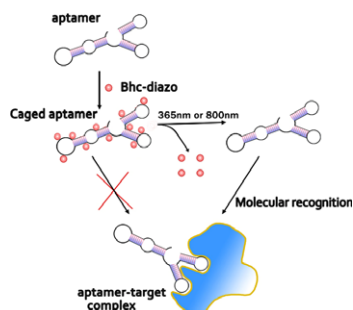


The design, synthesis and evaluation of a series of 4H-Pyrazolo[1,5-*a*]pyrimidin-7-ones as potent inhibitors of hepatitis C virus polymerase are described.

Photoregulation of thrombin aptamer activity using Bhc caging strategy

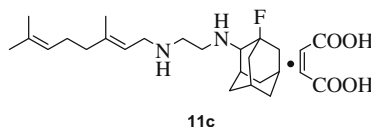
pp 5368–5371

YiMing Li, Jing Shi ^{*}, ZhaoFeng Luo, Hao Jiang, XiaoYun Chen, FengLiang Wang, Xu Wu, QingXiang Guo ^{*}

**Synthesis of novel [1,2]-diamines with antituberculosis activity**

pp 5372–5375

Qingyi Meng, Huibing Luo ^{*}, Yilang Chen, Tiancai Wang, Qizheng Yao ^{*}

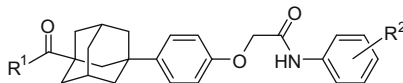


Guided by the metabolism information of **SQ109**, derivatives with substituted geranylamine moiety or substituted adamantane ring of **SQ109** were synthesized and evaluated as antituberculosis agents. Among all tested compounds, compound **11c** showed the most potent antituberculosis activity with MIC value of 0.3 μM against *Mycobacterium tuberculosis* H37Rv.

A novel class of highly potent multidrug resistance reversal agents: Disubstituted adamantyl derivatives

pp 5376–5379

Kyung Hoon Min^{*}, Yan Xia, Eun Kyung Kim, Yinglan Jin, Navneet Kaur, Eun Seon Kim, Dae Kyong Kim, Hwa Young Jung, Yongseok Choi, Mi-Kyung Park, Yong Ki Min, Kiho Lee, Kyeong Lee^{*}

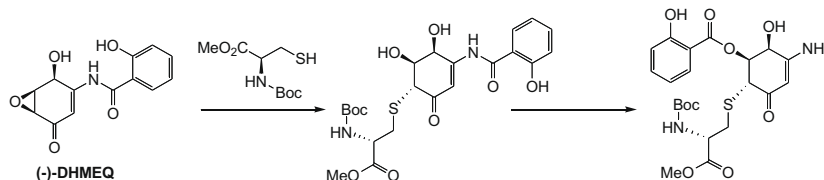


The synthesis and SAR of a new class of potent MDR reversal agents are reported.

Unusual intramolecular *N*→*O* acyl group migration occurring during conjugation of (–)-DHMEQ with cysteine

pp 5380–5382

Ikuko Kozawa, Kuniki Kato, Toshiaki Teruya, Kiyotake Suenaga, Kazuo Umezawa^{*}

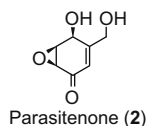


We observed an unusual intramolecular *N*→*O* acyl group migration in the course of formation of the (–)-DHMEQ and protected cysteine conjugate.

Efficient synthesis of (±)-parasitenone, a novel inhibitor of NF-κB

pp 5383–5386

Tsuyoshi Saitoh, Eriko Suzuki, Arisa Takasugi, Rika Obata, Yuichi Ishikawa, Kazuo Umezawa, Shigeru Nishiyama^{*}

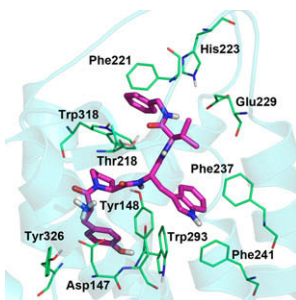


Parasitenone (2) was synthesized and the inhibitory activity against NF-κB was assessed.

Molecular modeling studies to predict the possible binding modes of endomorphin analogs in μ opioid receptor

pp 5387–5391

Xin Liu, Ming Kai, Lian Jin, Rui Wang^{*}



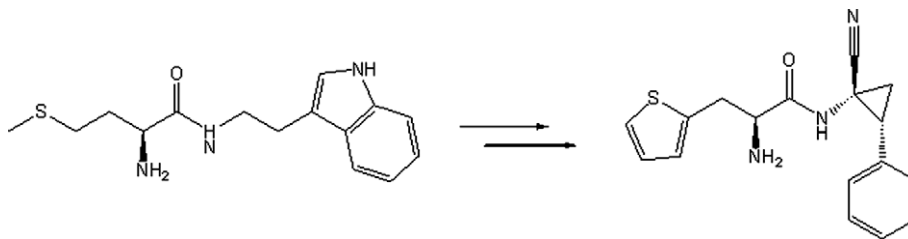
The binding mode of a series of endomorphin analogs in μ opioid receptor is predicted.



Design and synthesis of dipeptidyl nitriles as potent, selective, and reversible inhibitors of cathepsin C

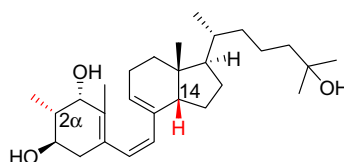
pp 5392–5396

Daniel Guay, Christian Beaulieu, T. Jagadeeswar Reddy, Robert Zamboni, Nathalie Methot, Joel Rubin, Diane Ethier, M. David Percival *

**Synthesis of 2 α -substituted-14-epi-previtamin D₃ and its genomic activity**

pp 5397–5400

Daisuke Sawada, Tomoyuki Katayama, Yuya Tsukuda, Nozomi Saito, Masashi Takano, Hiroshi Saito, Ken-ichiro Takagi, Eiji Ochiai, Seiichi Ishizuka, Kazuya Takenouchi, Atsushi Kittaka *

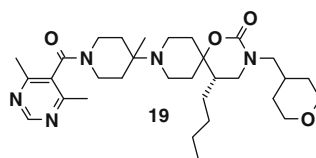


2 α -Substituted analogs of 14-epi-previtamin D₃ showed greater genomic activity than 14-epi-previtamin D₃ such as the VDR binding affinity and transactivation activity of osteocalcin promoter in HOS cells.

**Spiropiperidine CCR5 antagonists**

pp 5401–5406

David M. Rotstein *, Stephen D. Gabriel, Ferenc Makra, Lubov Filonova, Shelley Gleason, Christine Brotherton-Pleiss, Lina Q. Setti, Alejandra Trejo-Martin, Eun Kyung Lee, Surya Sankuratri, Changhua Ji, Andre deRosier, Marianna Dioszegi, Gabrielle Heilek, Andreas Jekle, Pamela Berry, Paul Weller, Cheng-I. Mau

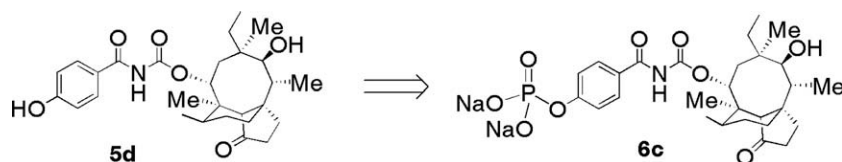


The discovery of a novel series of CCR5 small molecule antagonists is described. Lead optimization was pursued by balancing opposing trends of metabolic stability and potency. Selective and potent analogs with good pharmacokinetic properties were developed as exemplified by compound **19**.

Water-soluble phosphate prodrugs of pleuromutilin analogues with potent in vivo antibacterial activity against Gram-positive pathogens

pp 5407–5410

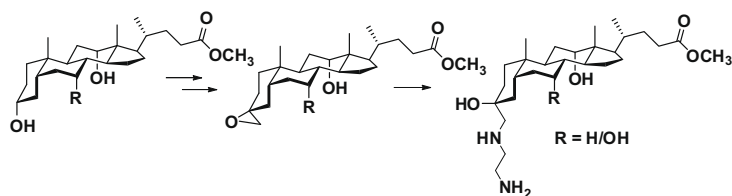
Liqiang Fu, Zhiteng Jiang, Zhan cai, Xin Liu, Huili He, Yushe Yang *



Synthesis and biological properties of phosphate prodrugs of pleuromutilin analogues are disclosed. Compound **6c** was metabolized efficiently to the biologically active parent **5d** in vivo, it also showed excellent antibacterial activity against MSSA and MRSA with comparable ED₅₀ as vancomycin by iv administration in mice.

Design and synthesis of bile acid-based amino sterols as antimicrobial agents

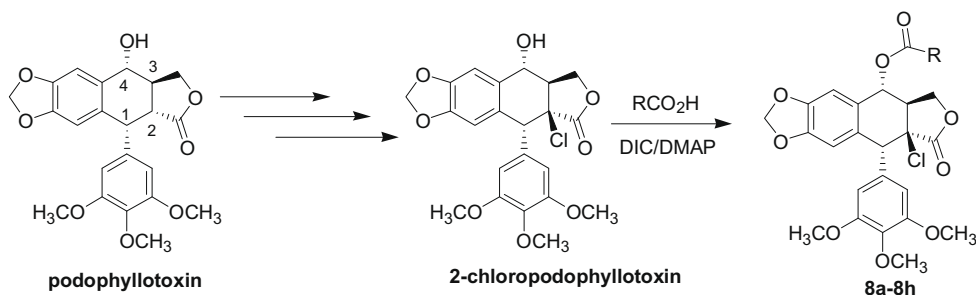
pp 5411–5414

Nilkanth G. Aher, Vandana S. Pore ^{*}, Nripendra N. Mishra, Praveen K. Shukla, Rajesh G. Gonnade

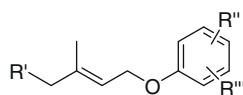
Aminosterols: antibacterial agents

**Natural products-based insecticidal agents 4. Semisynthesis and insecticidal activity of novel esters of 2-chloropodophyllotoxin against *Mythimna separata* Walker in vivo**

pp 5415–5418

Hui Xu ^{*}, Xiao Xiao**Prenyloxyphenylpropanoids as a novel class of anticonvulsive agents**

pp 5419–5422

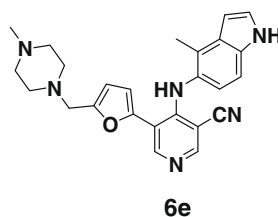
Salvatore Genovese, Francesco Epifano ^{*}, Massimo Curini, Monika Dudra-Jastrzebska, Jarogniew J. Luszczki

R' = H, isopentenyl, R'' = acetyl, COOH, CH=CH-COOH, α-O-CO-CH=CH-, R''' = H, OCH₃

The synthesis and neuroprotective activity (MES test) of selected prenyloxyphenylpropanoids is reported.

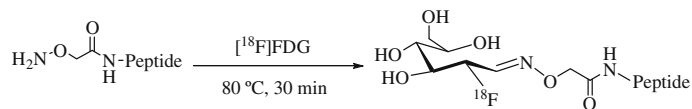
**C-5 Substituted heteroaryl 3-pyridinecarbonitriles as PKC θ inhibitors: Part I**

pp 5423–5425

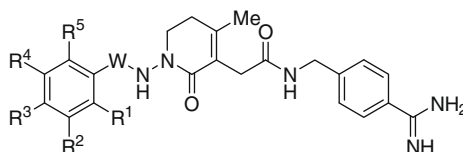
Joan Subrath ^{*}, Daniel Wang, Biqi Wu, Chuansheng Niu, Diane H. Boschelli, Julie Lee, Xiaoke Yang, Agnes Brennan, Divya ChaudharyAnalog **6e** with a 4-methylindol-5-ylamino group at C-4 and a 5-[(4-methylpiperazin-1-yl)methyl]-2-furyl group at C-5 had an IC₅₀ value of 4.5 nM for the inhibition of PKC.

Direct labelling of peptides with 2-[¹⁸F]fluoro-2-deoxy-D-glucose ([¹⁸F]FDG)

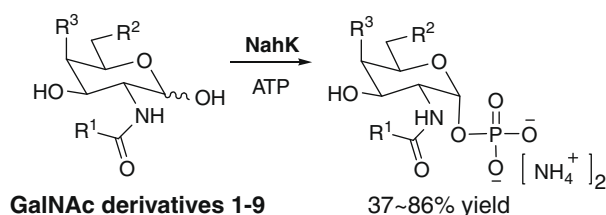
pp 5426–5428

Frank Wuest ^{*}, Christina Hultsch, Mathias Berndt, Ralf Bergmann**From natural products to achiral drug prototypes: Potent thrombin inhibitors based on P₂/P₃ dihydropyrid-2-one core motifs**

pp 5429–5432

Stephen Hanessian ^{*}, Eric Therrien, Jianbin Zhang, Willem van Otterlo, Yafeng Xue, David Gustafsson, Ingemar Nilsson ^{*}, Ola Fjellström**Substrate specificity of *N*-acetylhexosamine kinase towards *N*-acetylgalactosamine derivatives**

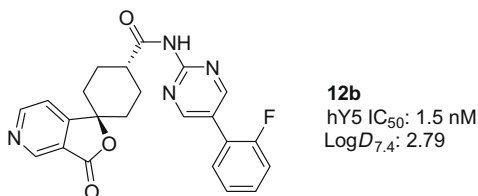
pp 5433–5435

Li Cai, Wanyi Guan, Wenjun Wang, Wei Zhao, Motomitsu Kitaoka, Jie Shen, Crystal O'Neil, Peng George Wang ^{*}

We report herein a bacterial *N*-acetylhexosamine kinase, NahK, with broad substrate specificity towards structurally modified GalNAc analogues, and the production of a GalNAc-1-phosphate library using this kinase.

**Identification of positron emission tomography ligands for NPY Y5 receptors in the brain**

pp 5436–5439

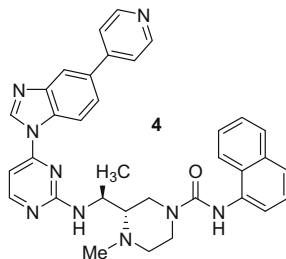
Hirobumi Takahashi, Yuji Haga, Takunobu Shibata, Katsumasa Nonoshita, Toshihiro Sakamoto, Minoru Moriya, Tomoyuki Ohe, Masato Chiba, Yuko Mitobe, Hidefumi Kitazawa, Hisashi Iwaasa, Akane Ishihara, Yasuyuki Ishii, Akio Kanatani, Takehiro Fukami ^{*}

Compound **12b** exhibited an acceptable profile for a PET ligand, and [¹¹C]**12b** was successfully utilized in clinical settings as a Y5 PET ligand.

Disubstituted pyrimidines as Lck inhibitors

pp 5440–5443

Julianne A. Hunt ^{*}, Richard T. Beresis, Joung L. Goulet, Mark A. Holmes, Xinfang J. Hong, Ernest Kovacs, Sander G. Mills, Rowena D. Ruzek, Frederick Wong, Jeffrey D. Hermes, Young-Whan Park, Scott P. Salowe, Lisa M. Sonatore, Lin Wu, Andrea Woods, Dennis M. Zaller, Peter J. Sinclair

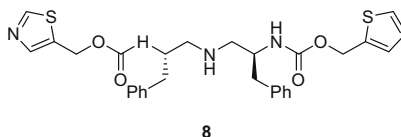


Compound **4** was found to be a potent inhibitor of Lck activity (IC_{50} = 0.1 nM) and cellular IL2 release (IC_{50} = 8 nM).

**Synthesis and evaluation of inhibitors of cytochrome P450 3A (CYP3A) for pharmacokinetic enhancement of drugs**

pp 5444–5448

Charles A. Flentge ^{*}, John T. Randolph, Peggy P. Huang, Larry L. Klein, Kennan C. Marsh, John E. Harlan, Dale J. Kempf

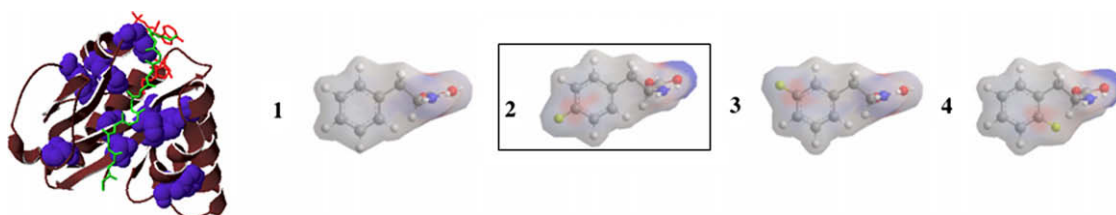


The structural elements of ritonavir were used to design a series of compounds which inhibit CYP3A. Compound **8** was found to strongly enhance plasma levels of lopinavir and compares favorably to ritonavir.

**Positional effects of monofluorinated phenylalanines on histone acetyltransferase stability and activity**

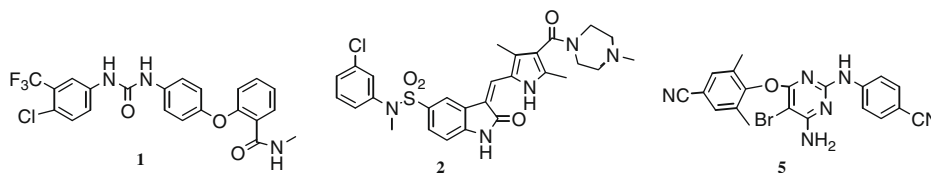
pp 5449–5451

Natalya Voloshchuk, Anita Y. Zhu, David Snyder, Jin Kim Montclare ^{*}

**Addressing the malaria drug resistance challenge using flow cytometry to discover new antimalarials**

pp 5452–5457

Brian T. Grimberg, Maria M. Jaworska, Lindsay B. Hough, Peter A. Zimmerman ^{*}, James G. Phillips ^{*}

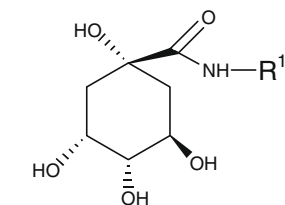


A new flow cytometry method that uses an optimized DNA and RNA staining strategy to monitor the growth and development of the *Plasmodium falciparum* strain W2mef has been used in a pilot study and has identified Bay 43-9006 **1**, SU 11274 **2**, and TMC 125 **5** as compounds that exhibit potent (<1 μ M) overall and ring stage in vitro antimalarial activity.

Synthesis and biological evaluation of quinic acid derivatives as anti-inflammatory agents

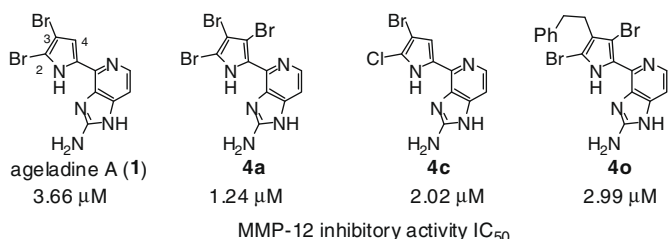
pp 5458–5460

Kui Zeng, Karin Emmons Thompson, Charles R. Yates, Duane D. Miller *

**Quinic Acid Derivatives****Synthesis of novel ageladine A analogs showing more potent matrix metalloproteinase (MMP)-12 inhibitory activity than the natural product**

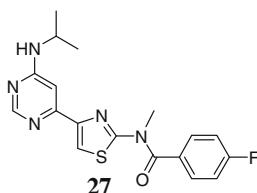
pp 5461–5463

Naoki Ando *, Shiro Terashima

The three ageladine A analogs **4a**, **c**, and **o** were found to show more potent MMP-12 inhibitory activity than natural ageladine A.**Discovery and in vitro and in vivo profiles of 4-fluoro-*N*-[4-[6-(isopropylamino)pyrimidin-4-yl]-1,3-thiazol-2-yl]-*N*-methylbenzamide as novel class of an orally active metabotropic glutamate receptor 1 (mGluR1) antagonist**

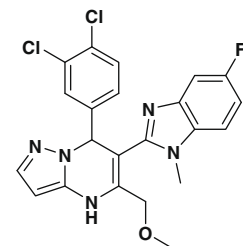
pp 5464–5468

Atsushi Satoh, Yasushi Nagatomi, Yukari Hirata, Satoru Ito, Gentaroh Suzuki, Toshifumi Kimura, Shunsuke Maehara, Hirohiko Hikichi, Akio Satow, Mikiko Hata, Hisashi Ohta, Hiroshi Kawamoto *

We identified 4-fluoro-*N*-[4-[6-(isopropylamino)pyrimidin-4-yl]-1,3-thiazol-2-yl]-*N*-methylbenzamide **27** as a potent mGluR1 antagonist. The compound possessed excellent subtype selectivity and good PK profile in rats. It also demonstrated relatively potent antipsychotic-like effects in several animal models.**Dihydropyrazolopyrimidines containing benzimidazoles as K_v1.5 potassium channel antagonists**

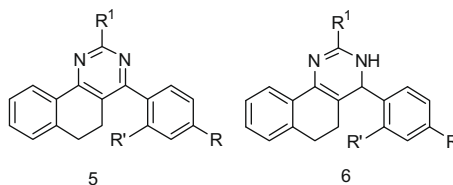
pp 5469–5473

John Lloyd *, Heather J. Finlay, Karnail Atwal, Alexander Kover, Joseph Prol, Lin Yan, Rao Bhandaru, Wayne Vaccaro, Tram Huynh, Christine S. Huang, MaryLee Conder, Tonya Jenkins-West, Huabin Sun, Danshi Li, Paul Levesque

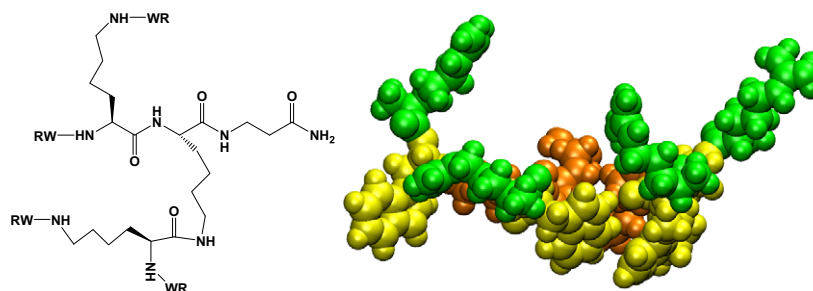
K_v1.5 blockers have the potential to be selective agents for the treatment of atrial fibrillation. Dihydropyrazolopyrimidines provide a template for the synthesis of potent and selective K_v1.5 blockers.**31a** K_v1.5 IC₅₀ 0.030 μM

Design and synthesis of novel substituted quinazoline derivatives as antileishmanial agents

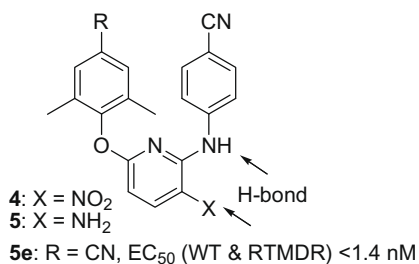
pp 5474–5477

K. C. Agarwal ^{*}, Vidisha Sharma, Nishi Shakya, Suman Gupta**Antimicrobial dendrimer active against *Escherichia coli* biofilms**

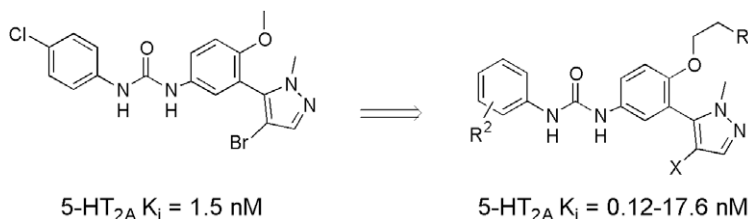
pp 5478–5481

Shuyu Hou, Chunhui Zhou, Zhigang Liu, Anne W. Young, Zhengshuang Shi, Dacheng Ren, Neville R. Kallenbach ^{*}**Discovery of diarylpyridine derivatives as novel non-nucleoside HIV-1 reverse transcriptase inhibitors**

pp 5482–5485

Xingtiao Tian, Bingjie Qin, Hong Lu, Weihong Lai, Shibo Jiang, Kuo-Hsiung Lee, Chin Ho Chen, Lan Xie ^{*}**Solubilized phenyl-pyrazole ureas as potent, selective 5-HT_{2A} inverse-agonists and their application as antiplatelet agents**

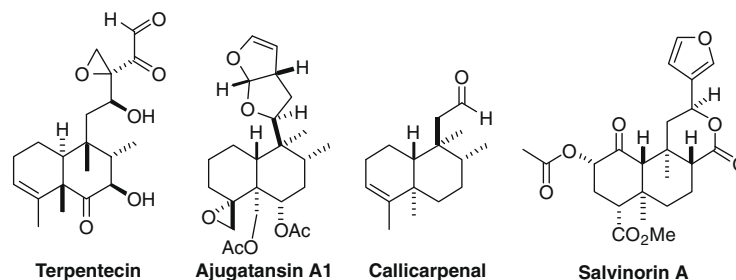
pp 5486–5489

Peter I. Dosa ^{*}, Sonja Strah-Pleyne, Honnappa Jayakumar, Martin Casper, Marc Decaire, Yifeng Xiong, Juerg Lehmann, Karoline Choi, Katie Elwell, Amy Wong, Robert R. Webb, John W. Adams, Juan Ramirez, Jeremy G. Richman, William Thomsen, Graeme Semple, Bradley R. Teegarden

Chemical methods for the synthesis and modification of neoclerodane diterpenes

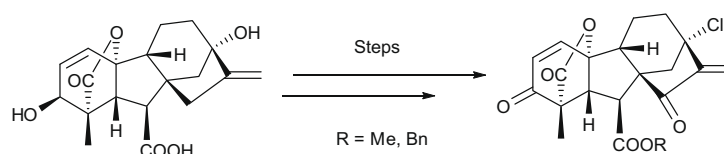
pp 5490–5495

Anthony Lozama, Thomas E. Prisinzano *

**Synthesis of gibberellin derivatives with anti-tumor bioactivities**

pp 5496–5499

Jingbo Chen, Zhuxian Sun, Yanli Zhang, Xianghui Zeng, Chen Qing *, Jianping Liu, Liang Li, Hongbin Zhang *

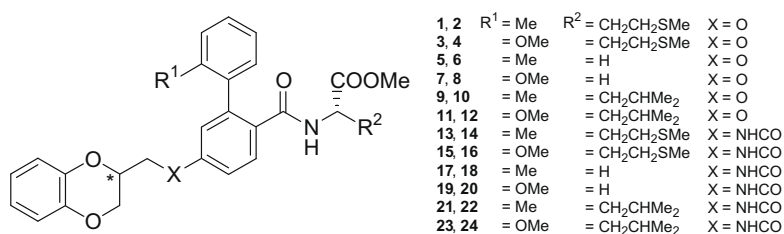


A series of gibberellin based molecules were designed and synthesized. Gibberellin derivatives bearing two α,β -unsaturated ketone units showed strong anticancer activities in MTT assay towards a number of human cancer cell lines including HT29, A549, HepG2 and MKN28. The most potent gibberellin derivative (R = Me, IC_{50} = 2.9 μ M against HT29) inhibited completely the topoisomerase I activity at 8 μ g/mL level.

New Ras CAAX mimetics: Design, synthesis, antiproliferative activity, and RAS prenylation inhibition

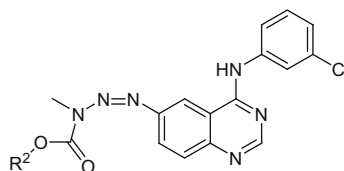
pp 5500–5504

Cristiano Bolchi, Marco Pallavicini, Laura Fumagalli, Nicola Ferri, Alberto Corsini, Chiara Rusconi, Ermanno Valoti *

**Design and synthesis of new stabilized combi-triazenes for targeting solid tumors expressing the epidermal growth factor receptor (EGFR) or its closest homologue HER2**

pp 5505–5509


Zakaria Rachid, Meaghan MacPhee, Christopher Williams, Margarita Todorova, Bertrand Jacques Jean-Claude *



The synthesis and biological activities of stabilized 3-alkyl-1,2,3-triazene-based EGFR-DNA targeting molecules are described.

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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