



Bioorganic & Medicinal Chemistry Letters Vol. 19, No. 7, 2009

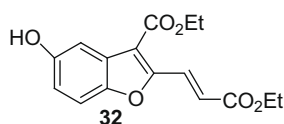
Contents

ARTICLES

Synthesis, discovery and preliminary SAR study of benzofuran derivatives as angiogenesis inhibitors

pp 1851–1854

Yuan Chen, Shaopeng Chen, Xin Lu, Hao Cheng, Yingyong Ou, Huimin Cheng, Guo-Chun Zhou *

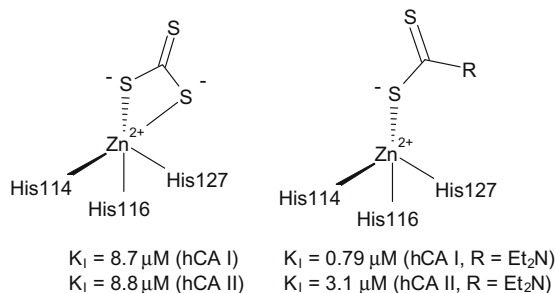


Compound **32** with benzofuran core exhibited good inhibitory activity ($IC_{50} = 4.3 \mu M$) and remarkable selectivity against HUVEC proliferation.

Carbonic anhydrase inhibitors. Inhibition of cytosolic isoforms I, II, III, VII and XIII with less investigated inorganic anions

pp 1855–1857

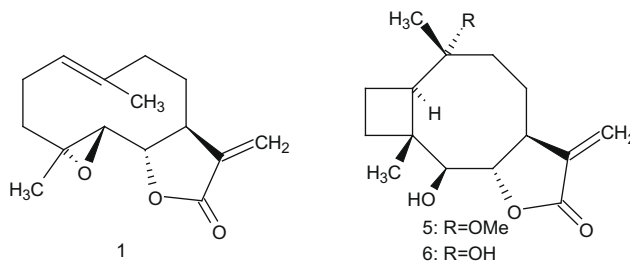
Alessio Innocenti, Andrea Scozzafava, Claudiu T. Supuran *



Inhibition of NF- κ B and metalloproteinase-9 expression and secretion by parthenolide derivatives

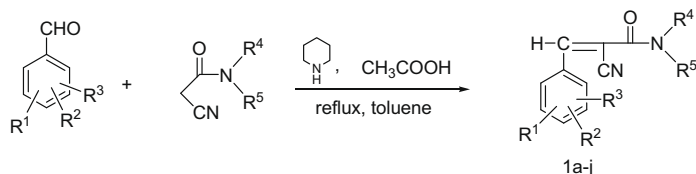
pp 1858–1860

Mario Dell'Agli *, Germana V. Galli, Enrica Bosisio, Michele D'Ambrosio



The synthesis and biological evaluation of some caffeic acid amide derivatives: *E*-2-Cyano-(3-substituted phenyl) acrylamides pp 1861–1865

Wei Zhou, Hai-bo Li, Chun-nian Xia, Xian-ming Zheng, Wei-xiao Hu *

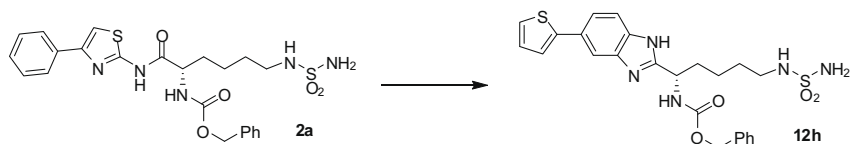


A series of caffeic acid amide derivatives *E*-2-cyano-(3-substituted phenyl) acrylamides were synthesized via Knoevenagel condensation. Some preliminary structure–activity relationships are described.



Synthesis and evaluation of lysine derived sulfamides as histone deacetylase inhibitors pp 1866–1870

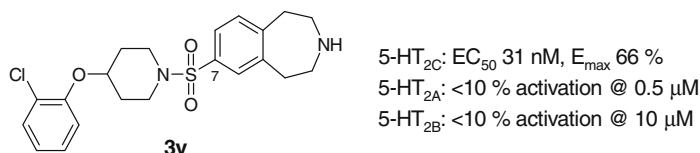
Sukhdev Manku, Martin Allan, Natalie Nguyen, Alain Ajamian, Jacques Rodrigue, Eric Therrien, James Wang, Tim Guo, Jubrail Rahil, Andrea J. Petschner, Alina Nicolescu, Sylvain Lefebvre, Zuomei Li, Marielle Fournel, Jeffrey M. Besterman, Robert Déziel, Amal Wahhab *



SAR investigation around compound **2a** lead to **12h** with equal HDAC1 and HDAC6 inhibitory activity and enhanced metabolic stability and PK profile.

7-Sulfonamido-3-benzazepines as potent and selective 5-HT_{2C} receptor agonists: Hit-to-lead optimization pp 1871–1875

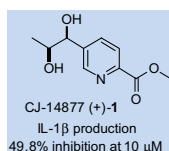
Paul V. Fish *, Alan D. Brown, Edel Evrard, Lee R. Roberts



New 7-sulfonamido-3-benzazepines **3** are disclosed as 5-HT_{2C} receptor agonists. Appropriate substitution of the amino group (R¹R²N-) identified compounds that were potent 5-HT_{2C} agonists with minimal activation of the 5-HT_{2A} and 5-HT_{2B} receptors. Furthermore, representative examples had excellent in vitro ADME properties and good selectivity over ion channel activity.

First asymmetric synthesis of CJ-14877 and its enantiomer and their interleukin-1β inhibitory activities pp 1876–1878

Yutaka Aoyagi, Yoshiyuki Adachi, Shunta Akagi, Naohito Ohno, Koichi Takeya *

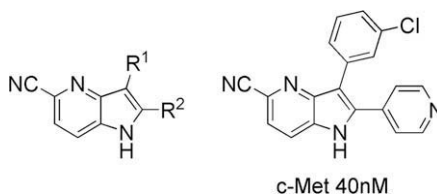


A potent antiinflammatory methyl picolinate alkaloid CJ-14877 [(+)-**1**] and its enantiomer (–)-**1** were synthesized via two steps. (+)-**1** strongly inhibited LPS-stimulated IL-1β production but (–)-**1** did not.

Syntheses of novel 2,3-diaryl-substituted 5-cyano-4-azaindoles exhibiting c-Met inhibition activity

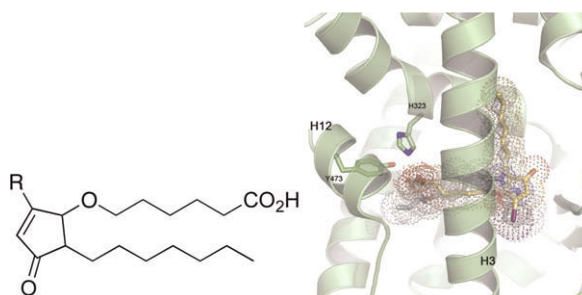
pp 1879–1882

Hannes Koolman*, Timo Heinrich, Henning Böttcher, Wilfried Rautenberg, Michael Reggelin

**Selective, potent PPAR γ agonists with cyclopentenone core structure**

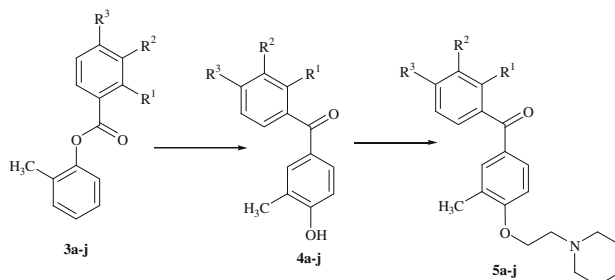
pp 1883–1886

M. Paz Otero, Efrén Pérez Santín, Fátima Rodríguez-Barrios, Belén Vaz, Ángel R. de Lera*

**Benzophenone-*N*-ethyl piperidine ether analogues—Synthesis and efficacy as anti-inflammatory agent**

pp 1887–1891

Shaukath A. Khanum*, V. Girish, S. S. Suparshwa, Noor Fatima Khanum

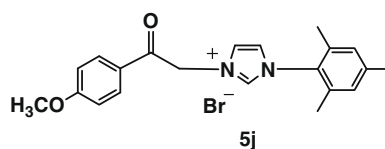


A sequence of substituted benzophenone-*N*-ethyl piperidine ether analogues has been synthesized and evaluated as orally active anti-inflammatory agents with reduced side effects.

Synthesis and cytotoxic activities of novel phenacylimidazolium bromides

pp 1892–1895

Xiao-Dong Yang, Xiang-Hui Zeng, Yan-Li Zhang, Chen Qing*, Wen-Jian Song, Liang Li, Hong-Bin Zhang*

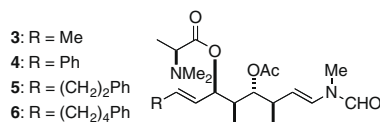


A series of novel phenacylimidazolium derivatives has been prepared and evaluated in vitro against a panel of human tumor cell lines. Phenacylimidazolium bromides bearing a highly sterically hindered aryl group at position-1 and an electron-rich phenacyl or naphthylacyl substituent at position-3 of imidazole ring proved to be more active than imidazolium bromides with other substituted groups. In particular, compound **5j** was found to be the most potent compounds with IC₅₀ values lower than 5.0 μ M against 8 strains human tumor cell lines and more active than cisplatin.

Synthesis of actin-depolymerizing compounds

pp 1896–1898

Kazuhiro Kitamura, Toshiaki Teruya, Takeshi Kuroda, Hideo Kigoshi, Kiyotake Suenaga *

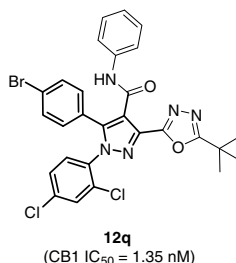


The artificial actin-depolymerizing compounds **3–6**, based on alyronine A, an actin-depolymerizing antitumor marine macrolide, were synthesized, and their actin-depolymerizing activities and cytotoxicities were evaluated.

Oxadiazole-diarylpyrazole 4-carboxamides as cannabinoid CB1 receptor ligands

pp 1899–1902

Suk Ho Lee, Hee Jeong Seo, Min Ju Kim, Suk Youn Kang, Kwang-Seop Song, Sung-Han Lee, Myung Eun Jung, Jeongmin Kim, Jinhwa Lee *

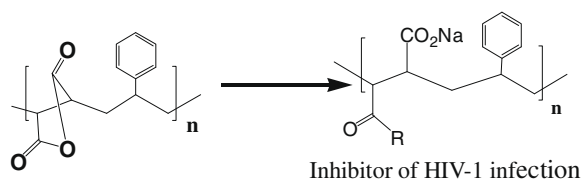


We have identified novel oxadiazole-diarylpyrazole 4-carboxamide series of small molecule cannabinoid-1 ligands that show potency comparable to that of known CB1 antagonists. Among various analogs tested, *N*-phenyl-4-carboxamide (**12q**) demonstrated high binding affinity for rCB1 receptor.

**Poly(styrene-*alt*-maleic anhydride) derivatives as potent anti-HIV microbicide candidates**

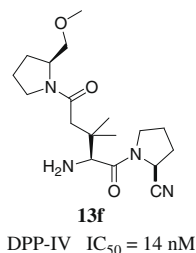
pp 1903–1907

Weijun Fang, Yijun Cai, Xiaoping Chen, Rongmin Su, Tong Chen, Ningshao Xia, Lei Li, Quanli Yang, Jiahuai Han *, Shoufa Han *

**Rational design and synthesis of potent and long-lasting glutamic acid-based dipeptidyl peptidase IV inhibitors**

pp 1908–1912

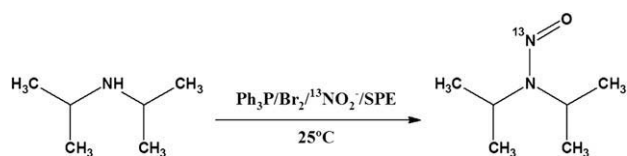
Ting-Yueh Tsai, Tsu Hsu, Chiung-Tong Chen, Jai-Hong Cheng, Mei-Chun Chiou, Chih-Hsiang Huang, Ya-Ju Tseng, Teng-Kuang Yeh, Chung-Yu Huang, Kai-Chia Yeh, Yu-Wen Huang, Ssu-Hui Wu, Min-Hsien Wang, Xin Chen, Yu-Sheng Chao, Weir-Torn Jiaang *



Efficient system for the preparation of [^{13}N]labeled nitrosamines

pp 1913–1915

Vanessa Gómez-Vallejo, Koichi Kato, Masayuki Hanyu, Katsuyuki Minegishi, José I. Borrell, Jordi Llop*

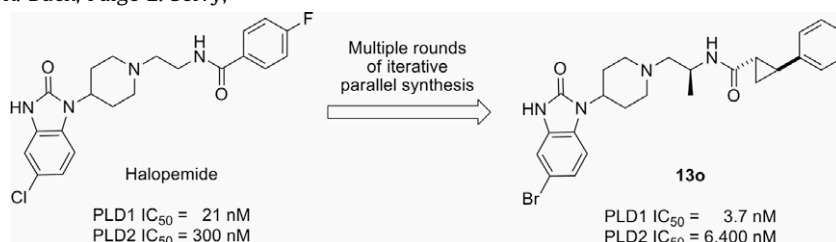


The reaction of resin trapped [^{13}N]NO $_2^-$ with secondary amines in the presence of Ph $_3$ P and Br $_2$ leads to the formation of the corresponding N-[^{13}N]nitrosamines with excellent radiochemical conversion.

Design and synthesis of isoform-selective phospholipase D (PLD) inhibitors. Part I: Impact of alternative halogenated privileged structures for PLD1 specificity

pp 1916–1920

Jana A. Lewis, Sarah A. Scott, Robert Lavieri, Jason R. Buck, Paige E. Selvy, Sydney L. Stoops, Michelle D. Armstrong, H. Alex Brown, Craig W. Lindsley*

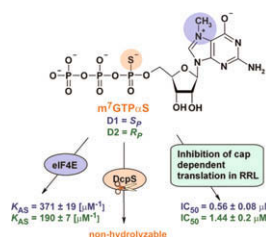


The synthesis and SAR of isoform-selective PLD inhibitors is described. By virtue of the installation of alternative halogenated piperidiny benzimidazolone privileged structures, in combination with a key (*S*)-methyl group, novel PLD inhibitors with low nM potency and unprecedented levels of isoform selectivity for PLD1 (~1700-fold) over PLD2 were developed.

Phosphorothioate analogs of m 7 GTP are enzymatically stable inhibitors of cap-dependent translation

pp 1921–1925

Joanna Kowalska, Maciej Lukaszewicz, Joanna Zuberek, Marcin Ziemiński, Edward Darzynkiewicz, Jacek Jemielity*

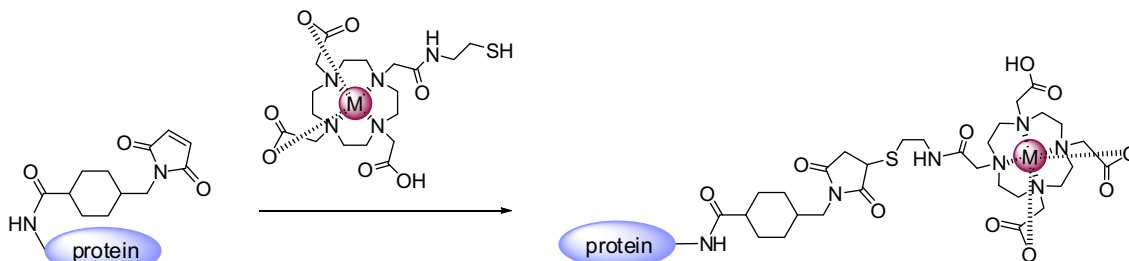


The synthesis and properties of new potent inhibitors of translation, two diastereomers of 7-methylguanosine 5'-(1-thiotriphosphate), are reported. These analogs of mRNA 5'cap are recognized by translational factor eIF4E with high affinity and are resistant to hydrolysis by Decapping Scavenger pyrophosphatase.

**Simple and convenient radiolabeling of proteins using a prelabeling-approach with thiol-DOTA**

pp 1926–1929

Carmen Wängler*, Ralf Schirmacher, Peter Bartenstein, Björn Wängler*

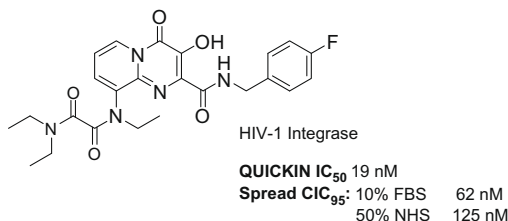


Prelabeled thiol-DOTA enables the efficient and simple introduction of radiometals into proteins under mild conditions.

3-Hydroxy-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxylates—A new class of HIV-1 integrase inhibitors

pp 1930–1934

Monica Donghi*, Olaf D. Kinzel, Vincenzo Summa

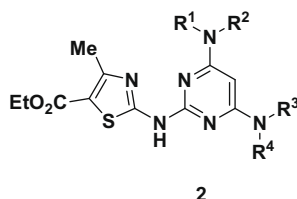


The synthesis and SAR of a new class of HIV-1 integrase inhibitors is reported.

Identification of potent pyrimidine inhibitors of phosphodiesterase 7 (PDE7) and their ability to inhibit T cell proliferation

pp 1935–1938

Junqing Guo*, Andrew Watson, James Kempson, Marianne Carlsen, Joseph Barbosa, Karen Stebbins, Deborah Lee, John Dodd, Steven G. Nadler, Murray McKinnon, Joel Barrish, William J. Pitts*

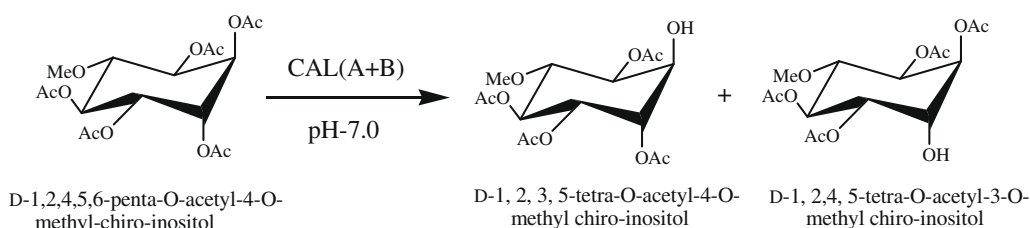


A series of pyrimidine based inhibitors of PDE7 are discussed. The synthesis, structure–activity relationships (SAR) and selectivity against several other PDE family members as well as activity in T cells are presented. These compounds were found to have effects on T cell proliferation, however it is not clear whether the mechanism is related to PDE7 inhibition.

Semi-synthetic analogs of pinitol as potential inhibitors of TNF- α cytokine expression in human neutrophils

pp 1939–1943

Khurshid A. Bhat, Bhahwal A. Shah, Kuldeep K. Gupta, Anjali Pandey, Sarang Bani, Subhash C. Taneja*

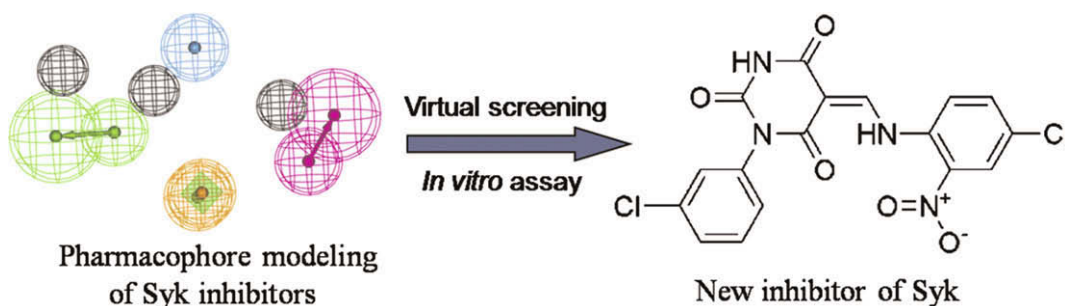


Semi-synthetic analogs of pinitol were prepared using chemo-enzymatic approaches and their TNF- α expression in human neutrophils using flowcytometry is reported.

Pharmacophore modeling study based on known Spleen tyrosine kinase inhibitors together with virtual screening for identifying novel inhibitors

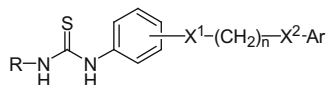
pp 1944–1949

Huan-Zhang Xie, Lin-Li Li, Ji-Xia Ren, Jun Zou, Li Yang, Yu-Quan Wei, Sheng-Yong Yang*



Design, synthesis, and anti-HCV activity of thiourea compounds**pp 1950–1955**

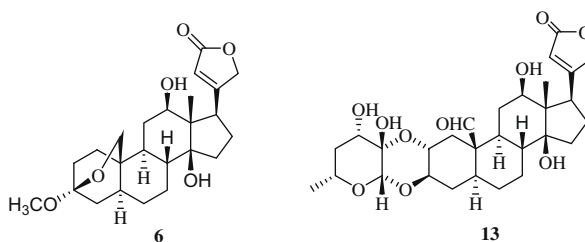
Iou-Jiun Kang, Li-Wen Wang, Chung-Chi Lee, Yen-Chun Lee, Yu-Sheng Chao, Tsu-An Hsu*, Jyh-Haur Chern*



The synthesis and SAR of potent hepatitis C virus inhibitors based on an aryl thiourea scaffold are described.

Cytotoxicity of cardenolides and cardenolide glycosides from *Asclepias curassavica***pp 1956–1959**

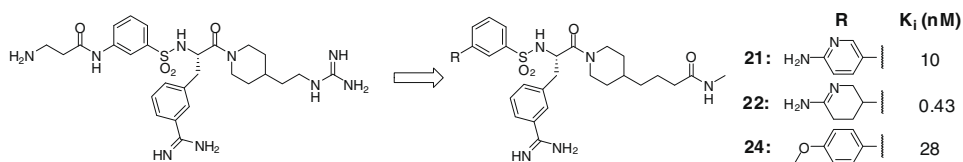
Jun-Zhu Li, Chen Qing, Chang-Xiang Chen, Xiao-Jiang Hao, Hai-Yang Liu*



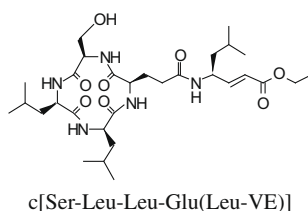
A new cardenolide **6** and a new doubly linked cardenolide glycoside **13** together with eleven known compounds were isolated from the aerial part of *Asclepias curassavica* and their cytotoxic activity was evaluated. The new compound **13** showed significant cytotoxic activity against HepG2 and Raji cell lines with IC₅₀ values of 0.69 and 1.46 μM, respectively.

Incorporation of neutral C-terminal residues in 3-amidinophenylalanine-derived matriptase inhibitors**pp 1960–1965**

Andrea Schweinitz, Daniel Dönnecke, Alexander Ludwig, Peter Steinmetzer, Alexander Schulze, Joscha Kotthaus, Silvia Wein, Bernd Clement, Torsten Steinmetzer*

**New cyclic peptide proteasome inhibitors****pp 1966–1969**

Anna Baldisserotto, Mauro Marastoni*, Riccardo Gavioli, Roberto Tomatis

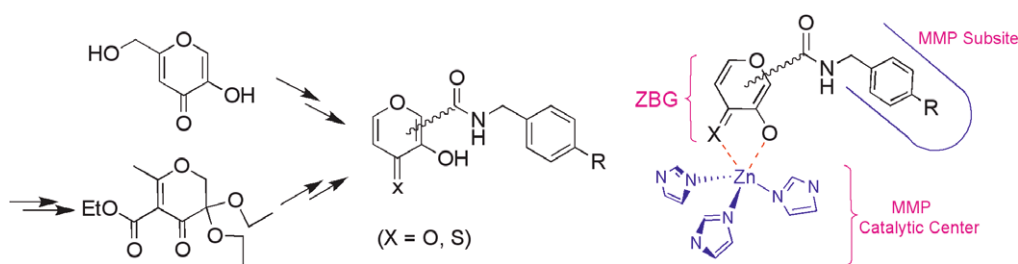


New vinyl ester cyclopeptide, derivatives were synthesized and tested as proteasome inhibitors. Some analogues showed selective inhibition of the β1 proteasome catalytic subunit.

Synthesis of hydroxypyrrone- and hydroxythiopyrrone-based matrix metalloproteinase inhibitors: Developing a structure–activity relationship

pp 1970–1976

Yi-Long Yan, Melissa T. Miller, Yuchen Cao, Seth M. Cohen*

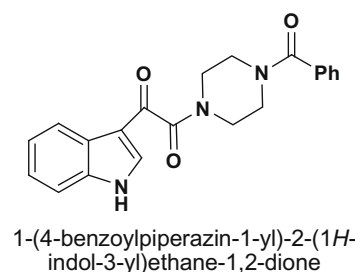


Inhibitors of HIV-1 attachment. Part 2: An initial survey of indole substitution patterns

pp 1977–1981

Nicholas A. Meanwell*, Owen B. Wallace, Haiquan Fang, Henry Wang, Milind Deshpande, Tao Wang, Zhiwei Yin, Zhongxing Zhang, Bradley C. Pearce, Jennifer James, Kap-Sun Yeung, Zhilei Qiu, J. J. Kim Wright, Zheng Yang, Lisa Zadjura, Donald L. Tweedie, Suresh Yeola, Fang Zhao, Sunanda Ranadive, Brett A. Robinson, Yi-Fei Gong, Hwei-Gene Heidi Wang, Wade S. Blair, Pei-Yong Shi, Richard J. Colonna, Pin-fang Lin

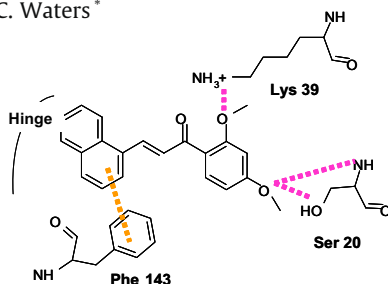
The effects of introducing simple halogen, alkyl, and alkoxy substituents to the 4, 5, 6 and 7 positions of 1-(4-benzoylpiperazin-1-yl)-2-(1*H*-indol-3-yl)ethane-1,2-dione, an inhibitor of the interaction between HIV gp120 and host cell CD4 receptors, on activity in an HIV entry assay was examined. Small substituents at C-4 generally resulted in increased potency whilst substitution at C-7 was readily tolerated and uniformly produced more potent HIV entry inhibitors. Substituents deployed at C-6 and, particularly, C-5 generally produced a modest to marked weakening of potency compared to the prototype. Small alkyl substituents at N-1 exerted minimal effect on activity whilst increasing the size of the alkyl moiety led to progressively reduced inhibitory properties. These studies establish a basic understanding of the indole element of the HIV attachment inhibitor pharmacophore.



Selective inhibition of Pfmrk, a *Plasmodium falciparum* CDK, by antimalarial 1,3-diaryl-2-propenones

pp 1982–1985

Jeanne A. Geyer, Susan M. Keenan, Cassandra L. Woodard, Philip A. Thompson, Lucia Gerena, Daniel A. Nichols, Clare E. Gutteridge, Norman C. Waters*



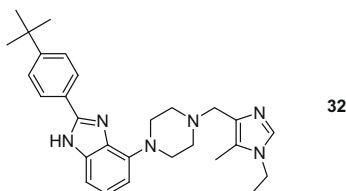
Various 1,3-diaryl-2-propenones which inhibit Pfmrk in the low micromolar range are identified. Modeling reveals two amino acid residues within the active site responsible for the selectivity over other CDKs.



Small molecule antagonists of the gonadotropin-releasing hormone (GnRH) receptor: Structure–activity relationships of small heterocyclic groups appended to the 2-phenyl-4-piperazinyl-benzimidazole template

pp 1986–1990

Diane B. Hauze*, Murty V. Chengalvala, Joshua E. Cottom, Irene B. Feingold, Lloyd Garrick, Daniel M. Green, Christine Huselton, Wenling Kao, Kenneth Kees, Joseph T. Lundquist IV, Charles W. Mann, John F. Mehlmann, John F. Rogers, Linda Shanno, Jay Wrobel, Jeffrey C. Pelletier



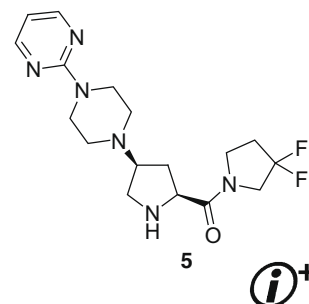
The potent GnRH antagonist template, 2-(4-*tert*-butylphenyl)-4-(1-piperazinyl)benzimidazole was appended to several small heterocycles. The *N*-ethylimidazole **32** was screened for in vivo pharmacokinetic and GnRH activity in rats.

(3,3-Difluoro-pyrrolidin-1-yl)-[(2S,4S)-(4-(4-pyrimidin-2-yl-piperazin-1-yl)-pyrrolidin-2-yl)-methanone]: A potent, selective, orally active dipeptidyl peptidase IV inhibitor

pp 1991–1995

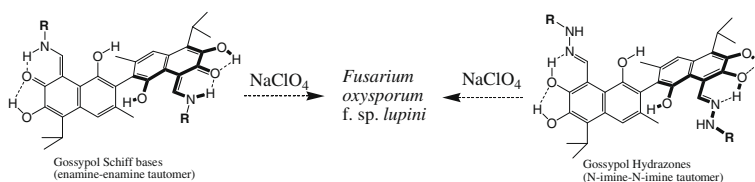
Mark J. Ammirati, Kim M. Andrews, David D. Boyer, Anne M. Brodeur, Dennis E. Danley, Shawn D. Doran, Bernard Hulin, Shenping Liu, R. Kirk McPherson, Stephen J. Orena, Janice C. Parker, Jana Polivkova, Xiayang Qiu, Carolyn B. Soglia, Judith L. Treadway, Maria A. VanVolkenburg, Donald C. Wilder, David W. Piotrowski*

A series of 4-substituted proline amides was evaluated as inhibitors of dipeptidyl peptidase IV for the treatment of type 2 diabetes. (3,3-Difluoro-pyrrolidin-1-yl)-[(2S,4S)-(4-(4-pyrimidin-2-yl-piperazin-1-yl)-pyrrolidin-2-yl)-methanone] (**5**) emerged as a potent ($IC_{50} = 13$ nM) and selective compound, with high oral bioavailability in preclinical species.

**Antifungal activity of alkyl and heterocyclic aza-derivatives of gossypol as well as their complexes with NaClO₄ against *Fusarium oxysporum* f. sp. *lupini***

pp 1996–2000

Piotr Przybylski*, Krystian Pyta, Dorota Remlein-Starosta, Grzegorz Schroeder, Bogumil Brzezinski, Franz Bartl

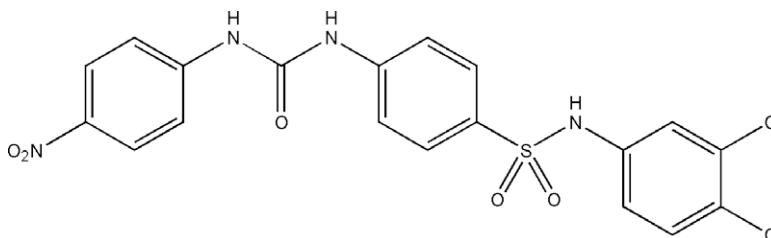


The antifungal tests after addition of NaClO₄ to gossypol aza-derivatives existing as the enamine–enamine tautomers and being the best ligands in complexation of Na⁺ cation or ClO₄[−] anion, indicated the improved activity of the complexes relatively to that of the pure compounds.

**Virtual screening to identify lead inhibitors for bacterial NAD synthetase (NADs)**

pp 2001–2005

Whitney Beysseance Moro, Zhengrong Yang, Tasha A. Kane, Christie G. Brouillette, Wayne J. Brouillette*

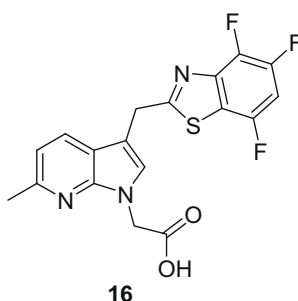


Structure-based virtual screening was used to identify new inhibitors of *Bacillus anthracis* nicotinamide adenine dinucleotide synthetase (NADs). 18 new small molecule inhibitors were identified with $IC_{50} \leq 100$ μ M, and a new lead structural class was chosen for optimization.

**Discovery of [3-(4,5,7-trifluoro-benzothiazol-2-ylmethyl)-pyrrolo[2,3-*b*]pyridin-1-yl]acetic acids as highly potent and selective inhibitors of aldose reductase for treatment of chronic diabetic complications**

pp 2006–2008

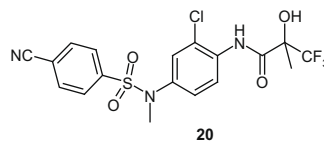
Michael C. Van Zandt*, Brian Doan, Diane R. Sawicki, Janet Sredy, Alberto D. Podjarny



Liver X receptor agonists with selectivity for LXR β ; N-aryl-3,3,3-trifluoro-2-hydroxy-2-methylpropionamides

pp 2009–2012

Britt-Marie Swahn*, Istvan Macsari, Jenny Viklund, Liselotte Öhberg, Johanna Sjödin, Jan Neelissen, Johanna Lindquist

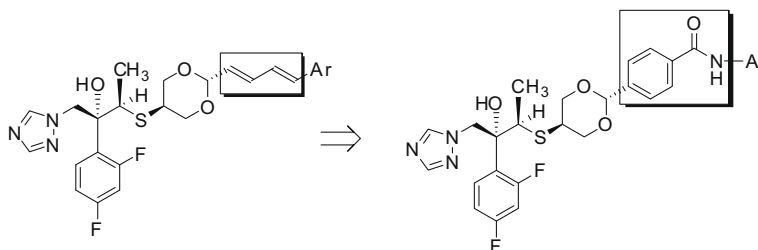


The synthesis and SAR of new liver X receptor agonists is reported. The effort to optimize these hits into LXR β selectivity is described. Compound **20** displayed desirable pharmacokinetic profile and was evaluated in vivo.

Amide analogs of antifungal dioxane–triazole derivatives: Synthesis and in vitro activities

pp 2013–2017

Takuya Uchida, Yoshiko Kagoshima, Toshiyuki Konosu*



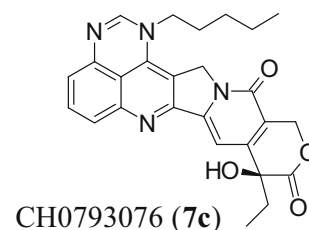
Synthesis and in vitro antifungal activities of a novel series of triazole antifungal agents wherein the diene part of CS-758 was replaced by an aryl-amide group are described.

Synthesis of new camptothecin analogs with improved antitumor activities

pp 2018–2021

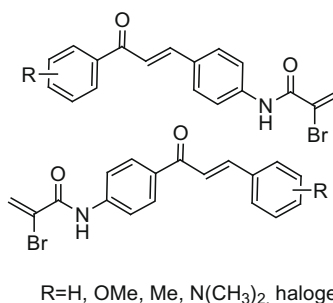
Satoshi Niizuma, Masao Tsukazaki, Hitomi Suda, Takeshi Murata, Jun Ohwada, Sawako Ozawa, Hiroshi Fukuda, Chikako Murasaki, Masami Kohchi, Kenji Morikami, Kiyoshi Yoshinari, Mika Endo, Masako Ura, Hiromi Tanimura, Yoko Miyazaki, Tsuyoshi Takasuka, Akira Kawashima, Eitaro Nanba, Kounosuke Nakano, Kotaro Ogawa, Kazuko Kobayashi, Hisafumi Okabe, Isao Umeda, Nobuo Shimma*

Design and synthesis of new topoisomerase I inhibitor, **7c** and its analogs, as well as their antitumor activities are described. Compound **7c** was effective against BCRP positive tumors.

**Hybrid α -bromoacryloylamido chalcones. Design, synthesis and biological evaluation**

pp 2022–2028

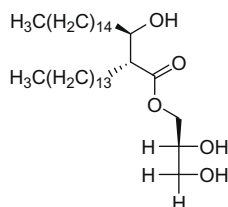
Romeo Romagnoli*, Pier Giovanni Baraldi*, Maria Dora Carrion, Olga Cruz-Lopez, Carlota Lopez Cara, Jan Balzarini, Ernest Hamel, Alessandro Canella, Enrica Fabbri, Roberto Gambari, Giuseppe Basso, Giampietro Viola



Adjuvant properties of a simplified C₃₂ monomycolyl glycerol analogue

pp 2029–2032

Veemal Bhowruth, David E. Minnikin, Else Marie Agger, Peter Andersen, Vincent W. Bramwell, Yvonne Perrie, Gurdial S. Besra *



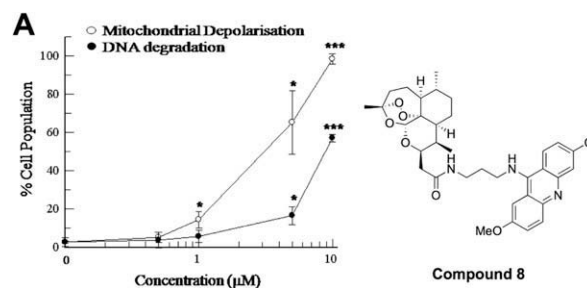
A C₃₂ monomycolyl glycerol analogue demonstrated elevated INF- γ and IL-6 levels, comparable to that of the potent Th1 adjuvant trehalose 6,6' di-behenate (TBD) in a dioctadecyl ammonium bromide (DDA)/Ag85B-ESAT-6 formulation.

Antitumour and antimalarial activity of artemisinin–acridine hybrids

pp 2033–2037

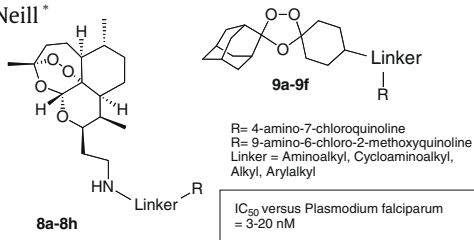
Michael Jones, Amy E. Mercer, Paul A. Stocks, Louise J. I. La Pensée, Rick Cosstick, B. Kevin Park, Miriam E. Kennedy, Ivo Piantanida, Stephen A. Ward, Jill Davies, Patrick G. Bray, Sarah L. Rawe *, Jonathan Baird, Tafadzwa Charidza, Omar Janneh, Paul M. O'Neill *

Artemisinin–acridine hybrids were prepared and evaluated for their in vitro activity against tumour cell lines and a chloroquine sensitive strain of *Plasmodium falciparum*. They showed a 2–4-fold increase in activity against HL60, MDA-MB-231 and MCF-7 cells in comparison with dihydroartemisinin (DHA) and moderate antimalarial activity. Strong evidence that the compounds induce apoptosis in HL60 cells was obtained by flow cytometry, which indicated accumulation of cells in the G1 phase of the cell cycle.

**Semi-synthetic and synthetic 1,2,4-trioxaquinones and 1,2,4-trioxolaquinones: synthesis, preliminary SAR and comparison with acridine endoperoxide conjugates**

pp 2038–2043

Nuna C. P. Araújo, Victoria Barton, Michael Jones, Paul A. Stocks, Stephen A. Ward, Jill Davies, Patrick G. Bray, Alison E. Shone, Maria L. S. Cristiano, Paul M. O'Neill *

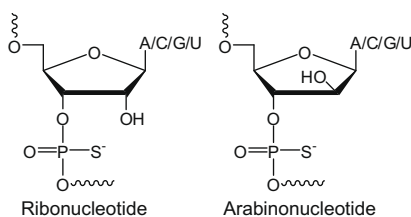


A series of semi-synthetic trioxaquinones and synthetic trioxolaquinones were prepared, in moderate to good yields, and were evaluated against both the chloroquine-sensitive 3D7 and resistant K1 strain of *Plasmodium falciparum*. For comparison the corresponding 9-amino acridine analogues were also prepared and shown to have low nanomolar activity like their quinoline counterparts.

Synthetic oligoribonucleotides containing arabinonucleotides act as agonists of TLR7 and 8

pp 2044–2047

Tao Lan, Lakshmi Bhagat, Daqing Wang, Meiru Dai, Ekambar R. Kandimalla, Sudhir Agrawal *



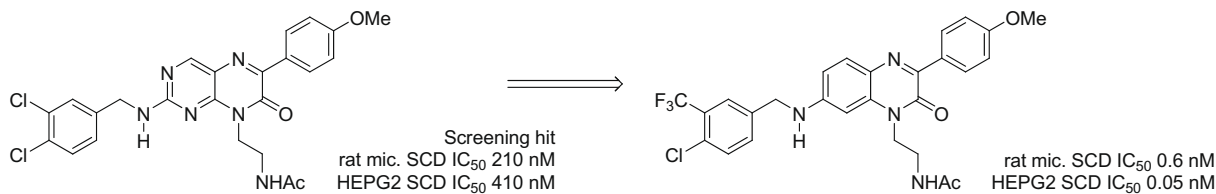
Oligoribonucleotides incorporating arabinonucleotides are synthesized and studied as agonists of Toll-like receptors 7 and 8.



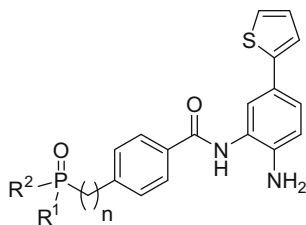
Novel, potent, selective, and metabolically stable stearyl-CoA desaturase (SCD) inhibitors

pp 2048–2052

Dmitry O. Koltun*, Eric Q. Parkhill, Natalya I. Vasilevich, Andrei I. Glushkov, Timur M. Zilbershtein, Alexei V. Ivanov, Andrew G. Cole, Ian Henderson, Nathan A. Zautke, Sandra A. Brunn, Nevena Mollova, Kwan Leung, Jeffrey W. Chisholm, Jeff Zablocki

**Exploring the pharmacokinetic properties of phosphorus-containing selective HDAC 1 and 2 inhibitors (SHI-1:2)** pp 2053–2058

Richard W. Heidebrecht Jr.* Melissa Chenard, Joshua Close, William K. Dahlberg, Judith Fleming, Jonathan B. Grimm, Julie E. Hamill, Andreas Harsch, Brian B. Haines, Bethany Hughes, Astrid M. Kral, Richard E. Middleton, Chandrasekhar Mushti, Nicole Ozerova, Alexander A. Szewczak, Hongmei Wang, Kevin Wilson, David J. Witter, J. Paul Secrist, Thomas A. Miller

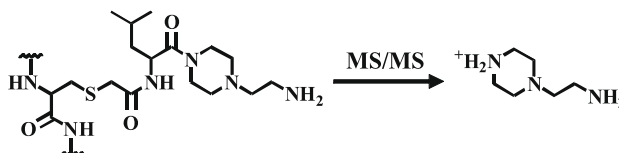


Preparation and structure–activity relationships of phosphorus-containing histone deacetylase inhibitors are detailed. A strong trend between decreasing phosphorus functional group size and superior mouse pharmacokinetic properties was identified. In addition, optimized candidates showed tumor growth inhibition in xenograft studies.

Improved CILAT reagents for quantitative proteomics

pp 2059–2061

Dexing Zeng, Shuwei Li*

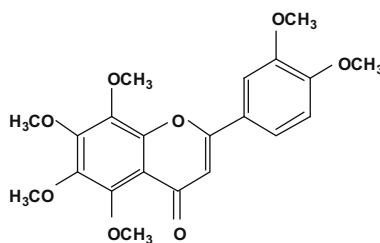


Novel stable isotope labeled reagents are synthesized, providing a robust tool for MS-based quantitative proteomics.

**Identification of nobiletin, a polymethoxyflavonoid, as an enhancer of adiponectin secretion**

pp 2062–2064

Kazuhiro Kunimasa, Sachi Kuranuki, Nobuyasu Matsuura, Nozomi Iwasaki, Megumi Ikeda, Akira Ito, Yutaka Sashida, Yoshihiro Mimaki, Masamichi Yano, Mayumi Sato, Yasuhiro Igarashi, Tsutomu Oikawa*

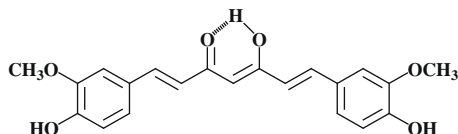


The identification of nobiletin as an enhancer of adiponectin secretion is reported.

Structure–activity relationship studies of curcumin analogues

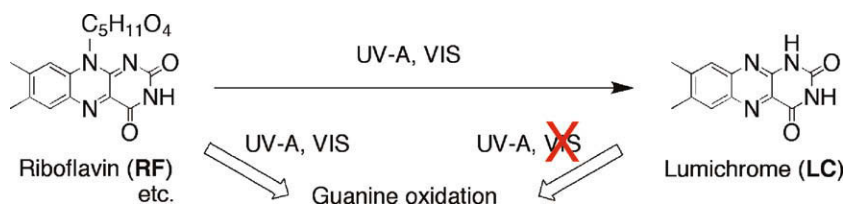
pp 2065–2069

James R. Fuchs, Bulbul Pandit, Deepak Bhasin, Jonathan P. Etter, Nicholas Regan,
Dalia Abdelhamid, Chenglong Li, Jiayuh Lin, Pui-Kai Li *

**Photoirradiation products of flavin derivatives, and the effects of photooxidation on guanine**

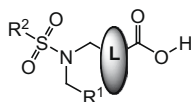
pp 2070–2074

Katsuhito Kino *, Teruhiko Kobayashi, Eiji Arima, Rie Komori, Takanobu Kobayashi, Hiroshi Miyazawa

**Discovery of CP-533536: An EP₂ receptor selective prostaglandin E₂ (PGE₂) agonist that induces local bone formation**

pp 2075–2078

Kimberly O. Cameron *, Bruce A. Lefker, Hua Z. Ke, Mei Li, Michael P. Zawistoski, Christina M. Tjoa, Ann S. Wright,
Shari L. DeNinno, Vishwas M. Paralkar, Thomas A. Owen, Li Yu, David D. Thompson

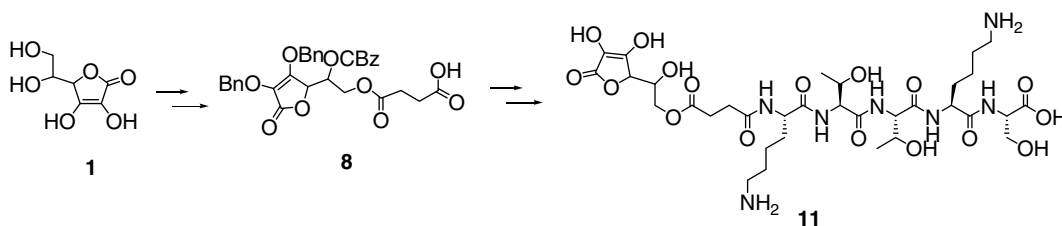


We describe the synthesis, SAR, and in vivo efficacy of a series of EP₂-selective sulfonamide derivatives.

Design and efficient synthesis of novel ascorbyl conjugated peptide with high collagen biosynthesis stimulating effects


pp 2079–2082

Ho-II Choi, Heung-Jae Kim, Jong-II Park, Eun-Ho Shin, Dong-Won Kim, Soung-Soo Kim *



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.]

Available online at

 **ScienceDirect**
www.sciencedirect.com

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

**ELSEVIER**

ISSN 0960-894X