

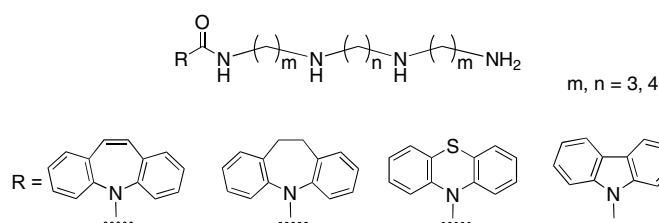
Contents

ARTICLES

Design, synthesis, and biological evaluation of tricyclic heterocycle-tetraamine conjugates as potent NMDA channel blockers

pp 4729–4732

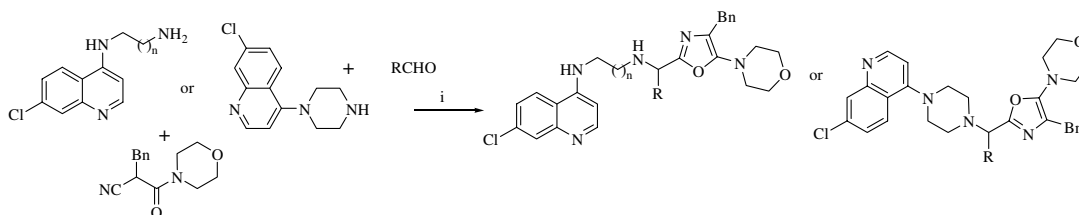
Hiromitsu Takayama,* Yuichi Yaegashi, Mariko Kitajima, Xia Han, Kazuhiro Nishimura, Shigeru Okuyama and Kazuei Igarashi*



Application of multicomponent reactions to antimalarial drug discovery. Part 3: Discovery of aminoxazole 4-aminoquinolines with potent antiplasmodial activity in vitro

pp 4733–4736

Chitalu C. Musonda, Susan Little, Vanessa Yardley and Kelly Chibale*



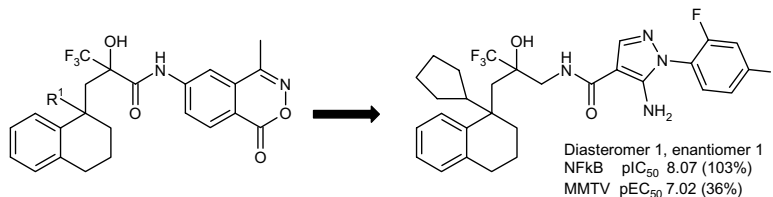
The synthesis and biological activity of a new series of 4-aminoquinoline-containing 2,4,5-trisubstituted aminoxazoles is described.



Non-steroidal glucocorticoid agonists—The discovery of aryl pyrazoles as A-ring mimetics

pp 4737–4745

Margaret Clackers, Diane M. Coe, Derek A. Demaine, George W. Hardy, Davina Humphreys, Graham G. A. Inglis, Michael J. Johnston, Haydn T. Jones, David House, Richard Loiseau, Doug J. Minick, Philip A. Skone, Iain Uings, Iain M. McLay and Simon J. F. Macdonald*

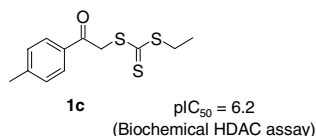


Based on a modelling and iterative approach, a potent dissociated glucocorticoid agonist was discovered where the benzoxazinone is replaced with an aryl pyrazole.

Trithiocarbonates—Exploration of a new head group for HDAC inhibitors

pp 4746–4752

Florian Dehmel,* Thomas Ciossek, Thomas Maier, Steffen Weinbrenner, Beate Schmidt, Martin Zoche and Thomas Beckers



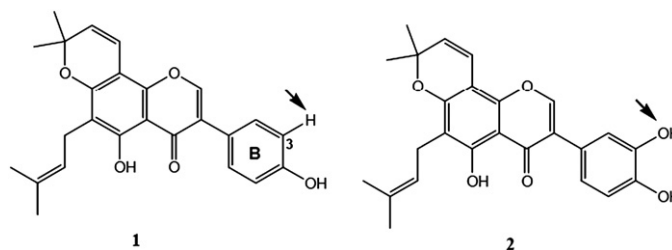
Trithiocarbonates are described as a new class of head groups for HDAC inhibition with biochemical and cellular activity.

Pomiferin, histone deacetylase inhibitor isolated from the fruits of *Maclura pomifera*

pp 4753–4755

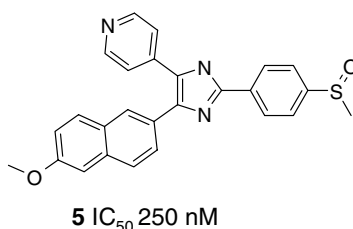
Il Hong Son, Ill-Min Chung, Sung Ik Lee, Hyun Duk Yang and Hyung-In Moon*

Pomiferin (**2**) was isolated from the fruits of *Maclura pomifera* as a potential histone deacetylase inhibitor. Its structure was determined by spectral and chemical methods. It inhibited histone deacetylase derived from PC-3 cell lines with GI_{50} values ranging from 3.78 μ M. Further structure–activity relationships of position 3 on ring B from aromatic ring will be reported in due course.

**Pyridinylimidazole inhibitors of Tie2 kinase**

pp 4756–4760

Marcus Semones,* Yanhong Feng, Neil Johnson, Jerry L. Adams, Jim Winkler and Michael Hansbury



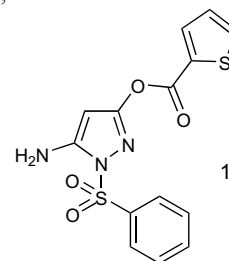
The synthesis and in-depth evaluation of compound **5**, an inhibitor ($IC_{50} = 250$ nM) of Tie2 kinase, is described.

Identification and characterization of 3-substituted pyrazolyl esters as alternate substrates for cathepsin B: The confounding effects of DTT and cysteine in biological assays

pp 4761–4766

Michael C. Myers, Andrew D. Napper, Nuzhat Motlekar, Parag P. Shah, Chun-Hao Chiu, Mary Pat Beavers, Scott L. Diamond, Donna M. Huryn* and Amos B. Smith, III*

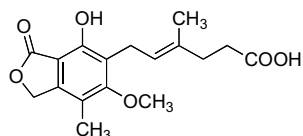
Substituted pyrazole esters were identified as hits in a high throughput screen (HTS) of the NIH Molecular Libraries Small Molecule Repository (MLSMR) to identify inhibitors of the enzyme cathepsin B. Members of this class, along with functional group analogs, were synthesized in an effort to define the structural requirements for activity. Analog characterization was hampered by the need to include a reducing agent such as dithiothreitol (DTT) or cysteine in the assay, highlighting the caution required in interpreting biological data gathered in the presence of such nucleophiles. Despite the confounding effects of DTT and cysteine, our studies demonstrate that the pyrazole **1** acts as alternative substrate for cathepsin B, rather than as an inhibitor.



Mycophenolic acid as a latent agonist of PPAR γ

pp 4767–4770

Makoto Ubukata,* Hitomi Takamori, Misaki Ohashi, Shinya Mitsuhashi, Kaoru Yamashita, Tomohisa Asada, Noriyuki Nakajima, Nobuyasu Matsuura, Mie Tsuruga, Keiko Taki and Junji Magae

Mycophenolic acid (**1**)

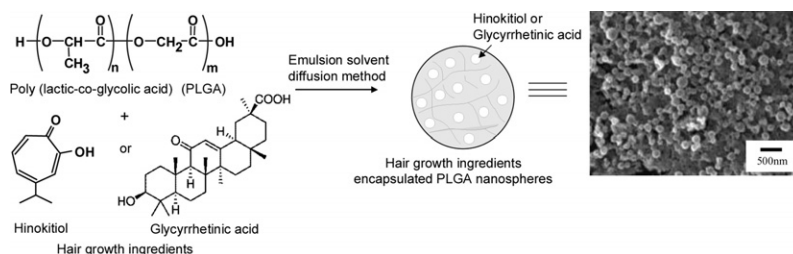
Mycophenolic acid (**1**), known as an inhibitor of inosine monophosphate dehydrogenase (IMPDH), was found to inhibit the differentiation of 3T3-L1 pre-adipocytes into mature adipocytes. Although the effect of **1** could be attributed to inhibition of IMPDH, we identified **1** as a latent agonist of PPAR γ . This is the first report that molecular target of **1** except IMPDH was found.

Evaluation of the permeability of hair growing ingredient encapsulated PLGA nanospheres to hair follicles and their hair growing effects

pp 4771–4777

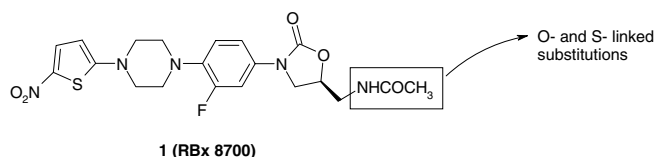
Hiroyuki Tsujimoto, Kaori Hara,* Yusuke Tsukada, C. C. Huang, Yoshiaki Kawashima, Minoru Arakaki, Hajime Okayasu, Haruko Mimura and Nobuhiko Miwa

The permeation of hair growing ingredients encapsulated in PLGA nanosphere having about 200 nm in mean particle size to the follicles of extracted human skin, and their effects on the fur growth of C3H mice, was evaluated. The PLGA nanospheres are useful carriers to deliver hair growing ingredients to follicles.

**Synthesis and antibacterial activity of novel oxazolidinones with methylene oxygen- and methylene sulfur-linked substituents at C5-position**

pp 4778–4783

Sonali Rudra,* Fnu Sangita, Arti Gujrati, Manisha Pandya, Pragya Bhateja, Tarun Mathur, Smita Singhal, Ashok Rattan, Mohammed Salman and Biswajit Das

**1 (RBx 8700)**

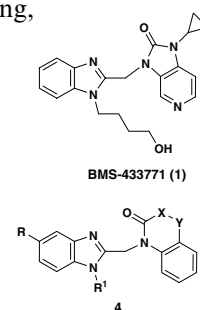
Novel oxazolidinone derivatives of the lead compound RBx 8700 containing methylene oxygen- and methylene sulfur-linked substituents at C5-position were synthesized and their biological activity reported.

Respiratory syncytial virus fusion inhibitors. Part 6: An examination of the effect of structural variation of the benzimidazol-2-one heterocycle moiety

pp 4784–4790

Keith D. Combrink, H. Belgin Gulgeze, Jan W. Thuring, Kuo-Long Yu, Rita L. Civiello, Yi Zhang, Bradley C. Pearce, Zhiwei Yin, David R. Langley, Kathleen F. Kadow, Christopher W. Cianci, Zhufang Li, Junius Clarke, Eugene V. Genovesi, Ivette Medina, Lucinda Lamb, Zheng Yang, Lisa Zadajura, Mark Krystal and Nicholas A. Meanwell*

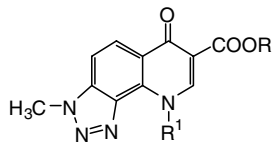
The effect of structural variation of the benzimidazol-2-one ring of RSV fusion inhibitors related to BMS-433771 (**1**) was examined in conjunction with side chain modifications and the introduction of an aminomethyl substituent at the 5-position of the core benzimidazole moiety. Replacement of the benzimidazol-2-one moiety with benzoxazole, oxindole, quinoline-2-one, quinazolin-2,4-dione and benzothiazine derivatives provided a series of potent RSV fusion inhibitors **4**. However, the intrinsic potency of 6,6-fused ring systems was generally less than that of comparably substituted 5,6-fused heterocycles of the type found in BMS-433771 (**1**). The introduction of an aminomethyl substituent to the benzimidazole ring enhanced antiviral activity in the 6,6-fused ring systems.



[1,2,3]Triazolo[4,5-*h*]quinolones. A new class of potent antitubercular agents against multidrug resistant *Mycobacterium tuberculosis* strains

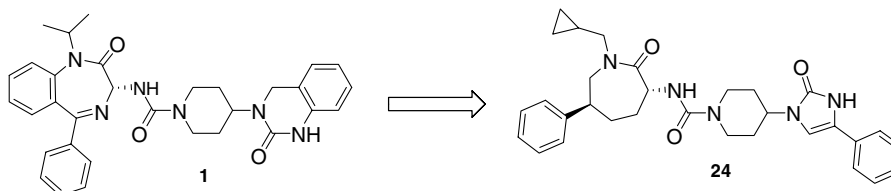
pp 4791–4794

Antonio Carta,* Michele Palomba, Giuseppe Paglietti, Paola Molicotti, Bianca Paglietti, Sara Cannas and Stefania Zanetti


Caprolactams as potent CGRP receptor antagonists for the treatment of migraine

pp 4795–4798

Anthony W. Shaw,* Daniel V. Paone, Diem N. Nguyen, Craig A. Stump, Christopher S. Burgey, Scott D. Mosser, Christopher A. Salvatore, Ruth Z. Rutledge, Stefanie A. Kane, Kenneth S. Koblan, Samuel L. Graham, Joeseeph P. Vacca and Theresa M. Williams

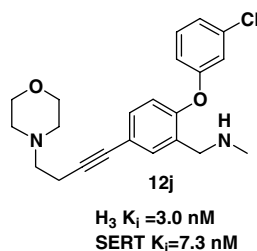


A series of (3*R*)-amino-(6*S*)-phenyl caprolactams were identified as benzodiazepine replacements for an early lead structure **1**. The syntheses and SAR studies leading to the discovery of **24** are described.

Benzylamine histamine H₃ antagonists and serotonin reuptake inhibitors

pp 4799–4803

Michael A. Letavic,* Emily M. Stocking, Ann J. Barbier, Pascal Bonaventure, Jamin D. Boggs, Brian Lord, Kirsten L. Miller, Sandy J. Wilson and Nicholas I. Carruthers



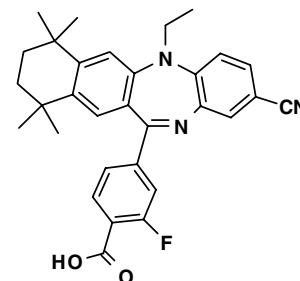
Novel benzyl amines are potent histamine H₃ antagonists and serotonin reuptake inhibitors.

Synthesis and structure–activity relationship of novel RXR antagonists: Orally active anti-diabetic and anti-obesity agents

pp 4804–4807

Junichi Sakaki, Masashi Kishida,* Kazuhide Konishi, Hiroki Gunji, Atsushi Toyao, Yuki Matsumoto, Takanori Kanazawa, Hidefumi Uchiyama, Hiroaki Fukaya, Hironobu Mitani, Yoshie Arai and Masaaki Kimura

A series of diazepinylbenzoic acid derivatives were synthesized and tested in the inhibition assay of the transactivation of RXR. Oral treatment of cyano derivatives showed anti-diabetic and anti-obesity effects in KK-A^y mice.

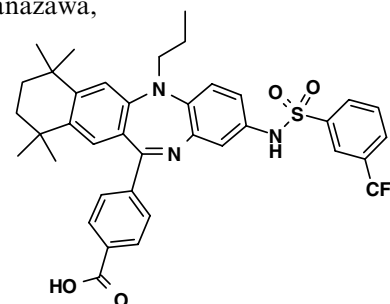


Synthesis and structure–activity relationship of RXR antagonists based on the diazepinylbenzoic acid structure

pp 4808–4811

Junichi Sakaki, Kazuhide Konishi, Masashi Kishida,* Hiroki Gunji, Takanori Kanazawa, Hidefumi Uchiyama, Hiroaki Fukaya, Hironobu Mitani and Masaaki Kimura

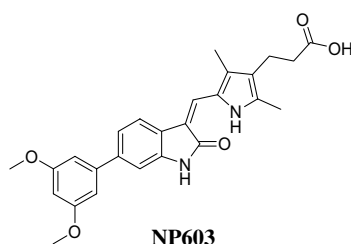
Synthesis and structure–activity relationship of RXR antagonists employing a diazepinylbenzoic acid scaffold are described. The sulfonamide derivatives were found to reveal a high antagonistic activity and good pharmacokinetic properties.



Novel inhibitor for fibroblast growth factor receptor tyrosine kinase

pp 4812–4818

Naparat Kammasud, Chantana Boonyarat, Satoshi Tsunoda, Hiroaki Sakurai,
Ikuo Saiki, David S. Grierson and Opa Vajragupta*

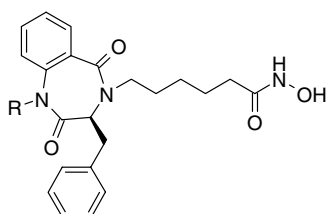


NP603 was designed as FGF receptor 1 inhibitor by computational study.

Design, synthesis and biological evaluation of 1,4-benzodiazepine-2,5-dione-based HDAC inhibitors

pp 4819–4823

Lynda Loudni, Joëlle Roche, Vincent Potiron, Jonathan Clarhaut, Christian Bachmann, Jean-Pierre Gesson and Isabelle Tranoy-Opalinski*



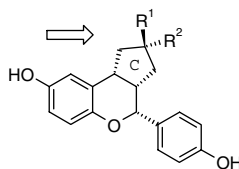
Hydroxamic acids containing 1,4-benzodiazepine-2,5-dione cap structures have been synthesized and evaluated for their antiproliferative and HDAC-inhibitory activities against H661 cancer cells.



Benzopyrans as selective estrogen receptor β agonists (SERBAs). Part 3: Synthesis of cyclopentanone and cyclohexanone intermediates for C-ring modification

pp 4824–4828

Timothy I. Richardson,* Jeffrey A. Dodge, Gregory L. Durst, Lance A. Pfeifer, Jikesh Shah, Yong Wang, Jim D. Durbin, Venkatesh Krishnan and Bryan H. Norman

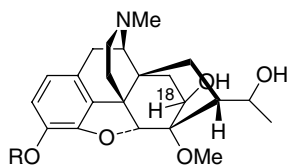


Structure activity relationship studies of the C-ring on the benzopyran scaffold are reported.

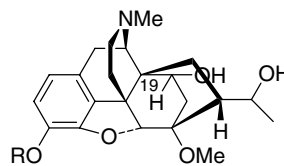
Functionalization of the 6,14-bridge of the orvinols. Part 3: Preparation and pharmacological evaluation of 18- and 19-hydroxyl substituted orvinols

pp 4829–4831

Huifang Wu, Trudy A. Smith, Hongyan Huang, Jia Bei Wang, Jeffrey R. Deschamps and Andrew Coop*



Partial mu opioid agonists



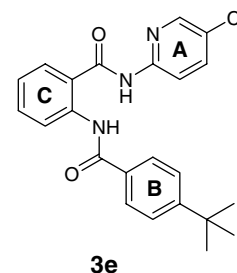
Full mu opioid agonists

Anthranilamide inhibitors of factor Xa

pp 4832–4836

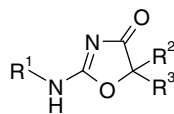
David Mendel,* Angela L. Marquart, Sajan Joseph, Philip Waid, Ying K. Yee, Anne Louise Tebbe, Andrew M. Ratz, David K. Herron, Theodore Goodson, John J. Masters, Jeffry B. Franciskovich, Jennifer M. Tinsley, Michael R. Wiley, Leonard C. Weir, Jeffrey A. Kyle, Valentine J. Klimkowski, Gerald F. Smith, Richard D. Towner, Larry L. Froelich, John Buben and Trelia J. Craft

SAR about the B-ring of *N*²-aroyl anthranilamide **3e** is described. B-ring *o*-aminoalkylethers and B-ring *p*-amine probes of the S1' and S4 sites, respectively, afforded picomolar factor Xa and nanomolar factor IIa inhibitors that were potent in in vitro anticoagulation assays.

**3e**
Oxazolones as potent inhibitors of 11 β -hydroxysteroid dehydrogenase type 1

pp 4837–4840

Lori Sutin,* Sören Andersson, Lars Bergquist, Victor M. Castro, Eva Danielsson, Stephen James, Martin Henriksson, Lars Johansson, Christina Kaiser, Katarina Flyrén and Meredith Williams

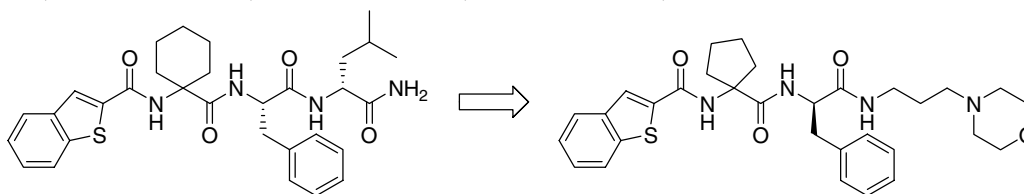
**1**

Compounds of general formula **1** were found to be potent inhibitors of 11 β -HSD1. Synthesis, structure–activity relationship and metabolic stability of these compounds are reported.

 α,α -Cyclic aminoacids as useful scaffolds for the preparation of hNK₂ receptor antagonists

pp 4841–4844

Alessandro Sisto, Maria Altamura, Franco Cardinali, Piero D'Andrea, Cristina Rossi and Daniela Fattori*

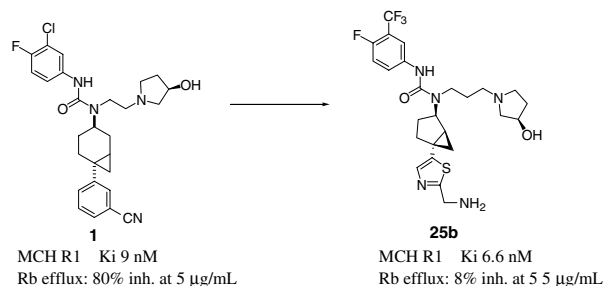
**1** pKi = 7.15 (hNK₂)**43** pKi = 9.2 (hNK₂)

In the search for a novel class of hNK₂ antagonists, compound **1** was identified from a tripeptide library. Subsequent optimization of binding affinity and physicochemical properties afforded **43**, subnanomolar hNK₂ antagonist.

Synthesis of novel bicyclo[4.1.0]heptane and bicyclo[3.1.0]hexane derivatives as melanin-concentrating hormone receptor R1 antagonists

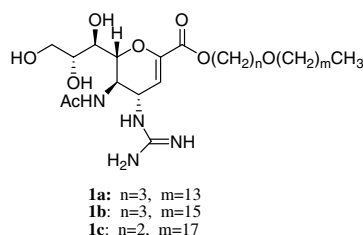
pp 4845–4850

Jing Su,* Haiqun Tang, Brian A. McKittrick, Huizhong Gu, Tao Guo, Gang Qian, Duane A. Burnett, John W. Clader, William J. Greenlee, Brian E. Hawes, Kim O'Neill, Brian Spar, Blair Weig, Timothy Kowalski and Steve Sorota

**Synthesis and anti-influenza activities of carboxyl alkoxyalkyl esters of 4-guanidino-Neu5Ac2en (zanamivir)**

pp 4851–4854

Zong-ying Liu, Bo Wang, Li-xun Zhao, Yu-huan Li, Hua-yi Shao, Hong Yi, Xue-fu You and Zhuo-rong Li*

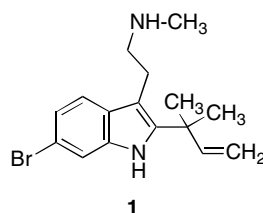


The modified analogs of zanamivir carboxylic moiety with alkoxyalkyl esters **1a–c** potentially inhibited influenza virus in cell culture and in mice.

Synthesis of desformylflustrabromine and its evaluation as an $\alpha 4\beta 2$ and $\alpha 7$ nACh receptor modulator

pp 4855–4860

Jin-Sung Kim, Anshul Padnya, Maegan Weltzin, Brian W. Edmonds, Marvin K. Schulte and Richard A. Glennon*

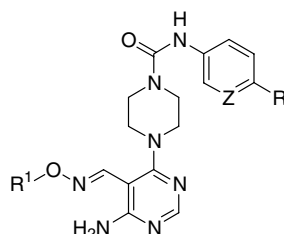


The present investigation reports the synthesis of desformylflustrabromine (dFBr; **1**) and desformylflustrabromine-B (dFBr-B; **2**) as their water-soluble hydrochloride salts and examines their action as positive allosteric modulators of $\alpha 4\beta 2$ nicotinic acetylcholine receptors using two-electrode voltage clamp recordings.

4-Amino-6-piperazin-1-yl-pyrimidine-5-carbaldehyde oximes as potent FLT-3 inhibitors

pp 4861–4865

Micheal D. Gaul,* Guozhang Xu, Jennifer Kirkpatrick, Heidi Ott and Christian A. Baumann

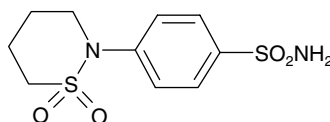


A series of 4-amino-6-piperazin-1-yl-pyrimidine-5-carbaldehyde oximes has been discovered and developed as potent FLT3 tyrosine kinase inhibitors. The series exhibited potent antiproliferative activity against both a FLT3 ITD-mutated human leukemic cell line as well as a wild-type FLT3 BaF₃ expressed cell line.

Carbonic anhydrase inhibitors. Interaction of the antiepileptic drug sulthiame with twelve mammalian isoforms: Kinetic and X-ray crystallographic studies

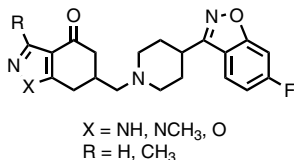
pp 4866–4872

Claudia Temperini, Alessio Innocenti, Antonio Mastrolorenzo, Andrea Scozzafava and Claudiu T. Supuran*


Synthesis and binding affinity of new pyrazole and isoxazole derivatives as potential atypical antipsychotics

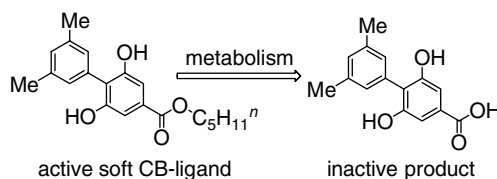
pp 4873–4877

María Barceló, Enrique Raviña, Christian F. Masaguer,* Eduardo Domínguez, Filipe Miguel Areias, José Brea and María I. Loza


Metabolically labile cannabinoid esters: A ‘soft drug’ approach for the development of cannabinoid-based therapeutic drugs

pp 4878–4881

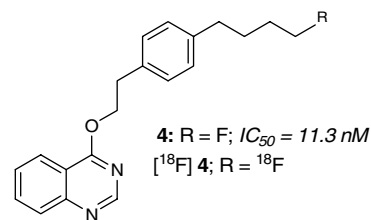
F. Minutolo,* M. G. Cascio, I. Carboni, T. Bisogno, G. Prota, S. Bertini, M. Digiacomo, M. Bifulco, V. Di Marzo and M. Macchia


Quinazoline derivatives as MC-I inhibitors: Evaluation of myocardial uptake using Positron Emission Tomography in rat and non-human primate

pp 4882–4885

Ajay Purohit,* Richard Benetti, Megan Hayes, Mary Guaraldi, Mikhail Kagan, Padmaja Yalamanchilli, Fran Su, Michael Azure, Mahesh Mistry, Ming Yu, Simon Robinson, Douglas D. Dischino and David Casebier

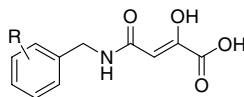
Several quinazoline derivatives based on fenazaquin were synthesized as highly potent MC-I inhibitors. One of these (shown above) was radiolabeled using ¹⁸F and was shown to have rapid uptake and retention in the heart.



Benzyl amide-ketoacid inhibitors of HIV-integrase

pp 4886–4890

Michael A. Walker,* Timothy Johnson, B. Narasimhulu Naidu, Jacques Banville, Roger Remillard, Serge Plamondon, Alain Martel, Chen Li, Albert Torri, Himadri Samanta, Zeyu Lin, Ira Dicker, Mark Krystal and Nicholas A. Meanwell

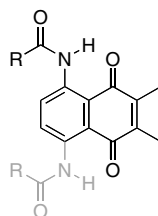


SAR study of benzyl amide-ketoacid based chemotype yielded highly active inhibitors of the HIV-integrase.

A relationship between amide hydrogen bond strength and quinone reduction potential: Implications for photosystem I and bacterial reaction center quinone function

pp 4891–4894

Ken S. Feldman,* D. Keith Hester, II and John H. Golbeck

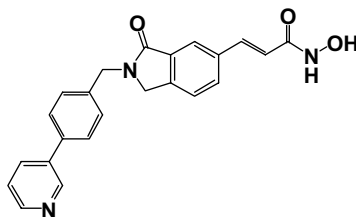


Peri-amide-substituted naphthoquinones were synthesized and their reduction potentials, N–H IR and N–H ¹H NMR absorptions were recorded.

**Design, synthesis, and evaluation of isoindolinone-hydroxamic acid derivatives as histone deacetylase (HDAC) inhibitors**

pp 4895–4900

Shoukou Lee, Chihiro Shinji, Kiyoshi Ogura, Motomu Shimizu, Satoko Maeda, Mayumi Sato, Minoru Yoshida, Yuichi Hashimoto and Hiroyuki Miyachi*



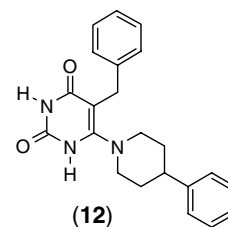
We designed and synthesized hydroxamic acid derivatives bearing a 4-(3-pyridyl)phenyl group as a cap structure, and found that they exhibit potent histone deacetylase (HDAC) inhibitory activity.

Discovery and optimization of novel, non-steroidal glucocorticoid receptor modulators

pp 4901–4905

Nicholas C. Ray,* Robin D. Clark, David E. Clark, Karen Williams, H. G. Hickin, Peter H. Crackett, Hazel J. Dyke, Peter M. Lockey, Melanie Wong, René Devos, Anne White and Joseph K. Belanoff

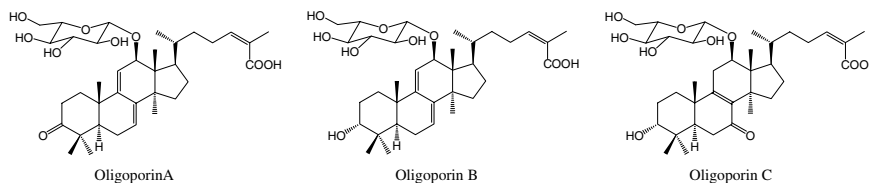
A virtual screening approach followed by lead optimization led to a series of compounds, exemplified by **12**, that were potent, selective GR antagonists.



New triterpene glucosides, oligoporins A–C, from *Oligoporus tephroleucus* protect DNA from Fenton reaction

pp 4906–4909

In-Kyoung Lee, Yun-Woo Jang, Seung Hun Yu and Bong-Sik Yun*

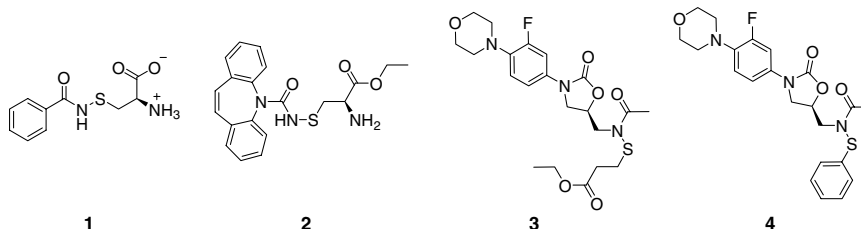


New triterpene glucosides, oligoporins A–C, protecting DNA from Fenton reaction, were isolated from the methanolic extract of the fruiting bodies of *Oligoporus tephroleucus*. Their structures were established by spectroscopic methods. These compounds significantly exhibited protective effect to plasmid DNA damage by hydroxyl radical (OH) generated from the Fenton reaction with hydrogen peroxide and ferrous.

Sulfenamides as prodrugs of NH-acidic compounds: A new prodrug option for the amide bond

pp 4910–4913

Victor R. Guarino, Veranja Karunaratne and Valentino J. Stella*



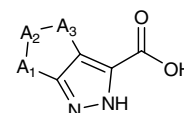
The objective of this report is to introduce the novel concept of utilizing sulfenamides as prodrugs for compounds containing an NH-acidic functionality, particularly weakly acidic amide-type functionalities.

Agonist lead identification for the high affinity niacin receptor GPR109a

pp 4914–4919

Tawfik Gharbaoui, Philip J. Skinner, Young-Jun Shin, Claudia Averbuj, Jae-Kyu Jung, Benjamin R. Johnson, Tracy Duong, Marc Decaire, Jane Uy, Martin C. Cherrier, Peter J. Webb, Susan Y. Tamura, Ning Zou, Nathalie Rodriguez, P. Douglas Boatman, Carleton R. Sage, Andrew Lindstrom, Jerry Xu, Thomas O. Schrader, Brian M. Smith, Ruoping Chen, Jeremy G. Richman, Daniel T. Connolly, Steven L. Colletti, James R. Tata and Graeme Semple*

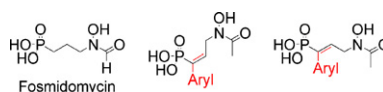
A strategy for lead identification of new agonists of GPR109a is described. Early compound triage led us to focus on a series of pyrazole acid derivatives. Further elaboration of these compounds provided a series of 5,5-fused pyrazoles to be used as lead compounds for further optimization.



Synthesis and evaluation of α,β -unsaturated α -aryl-substituted fosmidomycin analogues as DXR inhibitors

pp 4920–4923

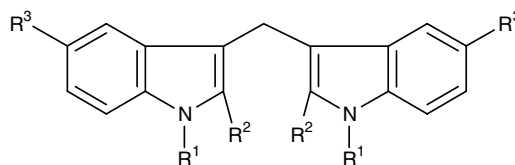
Vincent Devreux, Jochen Wiesner, Hassan Jomaa, Johan Van der Eycken and Serge Van Calenbergh*



Eco-friendly synthesis and study of new plant growth promoters: 3,3'-Diindolylmethane and its derivatives

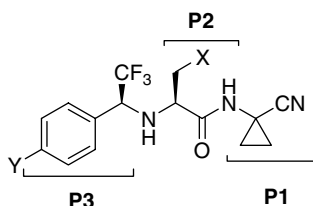
pp 4924–4928

Churala Pal, Sumit Dey, Sanjit Kumar Mahato, Jayaraman Vinayagam, Prasun K. Pradhan, Venkatachalam Sesha Giri, Parasuraman Jaisankar,* Tanvir Hossain, Shikhi Baruri, Debjit Ray and Suparna Mandal Biswas

**The identification of potent, selective, and bioavailable cathepsin S inhibitors**

pp 4929–4933

Jacques Yves Gauthier,* W. Cameron Black, Isabelle Courchesne, Wanda Cromlish, Sylvie Desmarais, Robert Houle, Sonia Lamontagne, Chun Sing Li, Frédéric Massé, Daniel J. McKay, Marc Ouellet, Joël Robichaud, Jean-François Truchon, Vouy-Linh Truong, Qingping Wang and M. David Percival

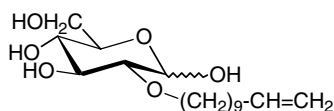


The Merck Frosst Centre for Therapeutic Research, 16711 Trans Canada Highway, Kirkland, Qué., Canada H9H 3L1.

Interaction of *O*-(undec-10-en)-yl-D-glucose derivatives with the *Plasmodium falciparum* hexose transporter (PfHT)

pp 4934–4937

Marina Ionita, Sanjeev Krishna, Pierre-Marc Léo, Christophe Morin* and Asha Parbhu Patel



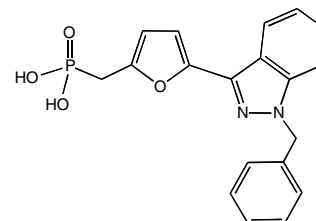
K_i (PfHT) = $2 \pm 0.3 \mu\text{M}$
 K_i (GLUT1) > 0.5 mM

Synthesis and evaluation of a phosphonate analogue of the soluble guanylate cyclase activator YC-1

pp 4938–4941

Nathaniel I. Martin, Emily R. Derbyshire and Michael A. Marletta*

The synthesis and testing of a phosphonate analogue of the soluble guanylate cyclase (sGC) activator YC-1 is described. With enhanced aqueous solubility, the effects of this analogue on sGC are reported.



YC-1 phosphonate analogue 5

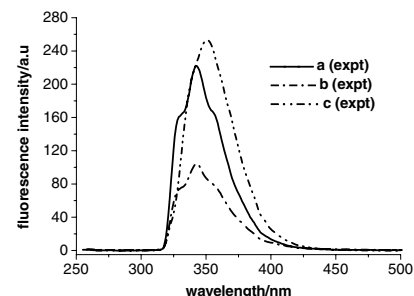
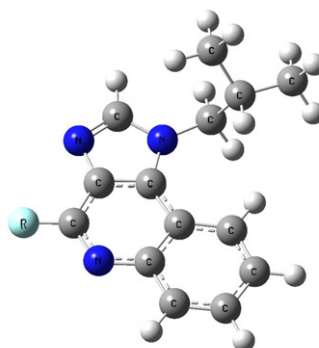


Experimental and theoretical study on the structure and electronic spectra of imiquimod and its synthetic intermediates

pp 4942–4946

Bo Zhao,* Yu-Zhi Rong, Xiao-Hua Huang and Jing-Shan Shen*

Fluorescence emission and UV–visible spectra, crystal structure, and DFT study of imiquimods a (R = H), b (R = Cl), and c (R = NH₂) were carried out in this work.

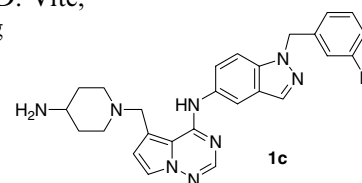


5-((4-Aminopiperidin-1-yl)methyl)pyrrolotriazine dual inhibitors of EGFR and HER2 protein tyrosine kinases

pp 4947–4954

Harold Mastalerz,* Ming Chang, Ping Chen, Brian E. Fink, Ashvinikumar Gavai, Wen-Ching Han, Walter Johnson, David Langley, Francis Y. Lee, Kenneth Leavitt, Punit Marathe, Derek Norris, Simone Oppenheimer, Bogdan Slecza, James Tarrant, John S. Tokarski, Gregory D. Vite, Dolatrai M. Vyas, Henry Wong, Tai W. Wong, Hongjian Zhang and Guifen Zhang

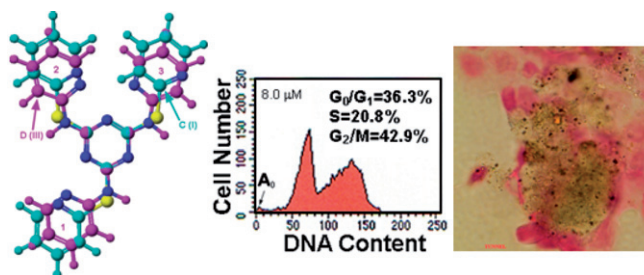
5-((4-Aminopiperidin-1-yl)methyl)-pyrrolotriazine dual EGFR and HER2 protein tyrosine kinase inhibitor, **1c**, exhibited potent kinase inhibition, antiproliferative activity, and good oral efficacy in a EGFR/HER2 driven human tumor xenograft models. A broad range of potent pyrrolotriazine dual EGFR and HER2 kinase inhibitors are possible with the C5 aminopiperidine solubilizing group.



A novel series of potent cytotoxic agents targeting G2/M phase of the cell cycle and demonstrating cell killing by apoptosis in human breast cancer cells

pp 4955–4960

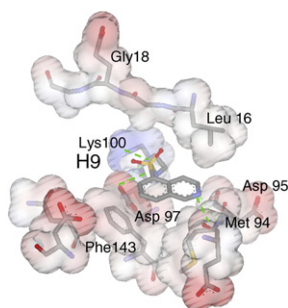
Soma Mandal, Gervais Bérubé, Éric Asselin, Iqbal Mohammad, Vernon J. Richardson, Atul Gupta, Saroj K. Pramanik, Arthur L. Williams and Sanat K. Mandal*



Evaluation of broad spectrum protein kinase inhibitors to probe the architecture of the malarial cyclin dependent protein kinase Pfmrk

pp 4961–4966

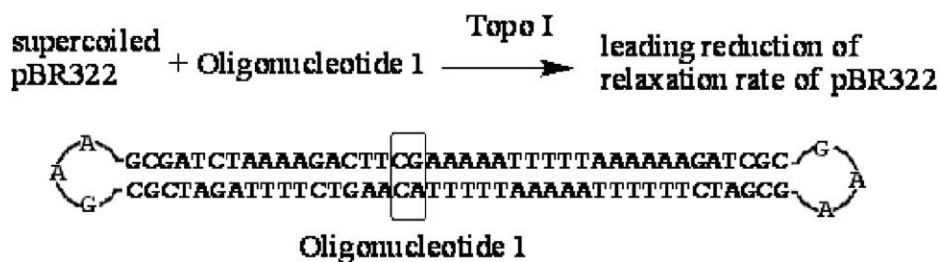
Cassandra L. Woodard, Susan M. Keenan, Lucia Gerena, William J. Welsh, Jeanne A. Geyer and Norman C. Waters*



Dumbbell-shaped circular oligonucleotides as inhibitors of human topoisomerase I

pp 4967–4971

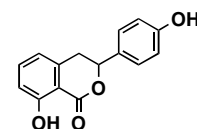
Xinming Li, Magdeline Tao Tao Ng, Yifan Wang, Xiaoqian Liu and Tianhu Li*

**New type of anti-diabetic compounds from the processed leaves of *Hydrangea macrophylla* var. *thunbergii* (Hydrangeae Dulcis Folium)**

pp 4972–4976

Hailong Zhang, Hisashi Matsuda, Akira Kumahara, Yuki Ito, Seikou Nakamura and Masayuki Yoshikawa*

Two 3-phenyldihydroisocoumarins (hydrangenol and phyllodulcin), a 3-phenylisocoumarin (thunberginol A), and a stilbene (hydrangeic acid) from the processed leaves of *Hydrangea macrophylla* var. *thunbergii* (Hydrangeae Dulcis Folium) promoted adipogenesis of 3T3-L1 cells. Hydrangenol, a principal constituent, significantly increased the amount of adiponectin released into the medium and mRNA levels of adiponectin, peroxisome proliferator-activated receptor γ 2 (PPAR γ 2), and glucose transporter 4 (GLUT4), while it decreased the expression of interleukin 6 (IL-6) mRNA. Furthermore, hydrangenol significantly lowered blood glucose and free fatty acid levels 2 weeks after its administration at a dose of 200 mg/kg/d in KK-A y mice.

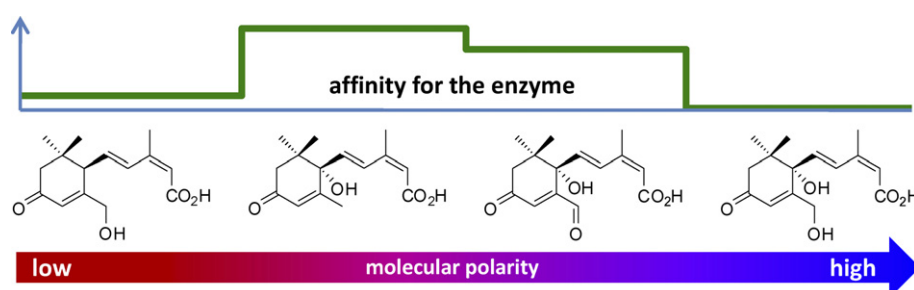


hydrangenol

Effect of the minor ABA metabolite 7'-hydroxy-ABA on Arabidopsis ABA 8'-hydroxylase CYP707A3

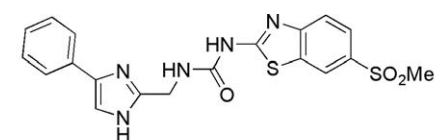
pp 4977–4981

Hajime Shimomura, Hideo Etoh, Masaharu Mizutani, Nobuhiro Hirai and Yasushi Todoroki*

**Phenylimidazole derivatives as new inhibitors of bacterial enoyl-ACP reductase FabK**

pp 4982–4986

Hideo Kitagawa,* Tomohiro Ozawa, Sho Takahata and Maiko Iida



Streptococcus pneumoniae FabK IC₅₀ 0.14 μ M
MIC 0.5 μ g/mL

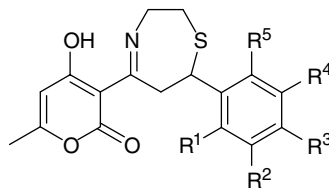
We discovered the phenylimidazole derivative as a novel inhibitor of bacterial enoyl-ACP reductase (FabK). It selectively exhibited strong FabK-inhibitory activity and good antibacterial activities against *Streptococcus pneumoniae*.



Discovery of 5-(4-hydroxy-6-methyl-2-oxo-2H-pyran-3-yl)-7-phenyl-(E)-2,3,6,7-tetrahydro-1,4-thiazepines as a new series of apoptosis inducers using a cell- and caspase-based HTS assay

pp 4987–4990

John Drewe, Shailaja Kasibhatla, Ben Tseng, Emma Shelton, David Sperandio, Robert M. Yee, Joane Litvak, Martin Sendzik, Jeffrey R. Spencer and Sui Xiong Cai*

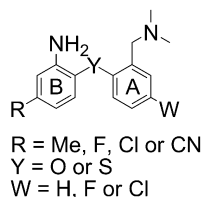


The discovery and SAR studies of 5-(4-hydroxy-6-methyl-2-oxo-2H-pyran-3-yl)-7-phenyl-(E)-2,3,6,7-tetrahydro-1,4-thiazepines as a novel series of apoptosis inducers is reported.

New fluoro-diphenylchalcogen derivatives to explore the serotonin transporter by PET

pp 4991–4995

Johnny Vercouillie,* Winnie Deuther-Conrad, Matthias Scheunemann, Patrick Emond, Steffen Fischer, Uta Funke, Jörg Steinbach, Denis Guilloteau and Peter Brust



The synthesis of highly potent fluorinated SERT tracers is reported.



OTHER CONTENTS

Summary of instructions to authors

p I

*Corresponding author

Supplementary data available via ScienceDirect

COVER

Typical snapshot of **7b** bound to HIV-RT from an MC simulation. Carbon atoms of **7b** are gold; from the left, Tyr181, Tyr188, Phe227, Leu100, Lys101; Trp229 at the top, Val106 at the bottom. H-bond with Lys101 O on right. Some residues in front including Glu138 have been removed for clarity. The water on N5 is also H-bonded to a carboxylate O of Glu138. [Thakur, V. T.; Kim, J. T.; Hamilton, A. D.; Bailey, C. M.; Domaoal, R. A.; Wang, L.; Anderson, K. S.; Jorgensen, W. L. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5664.]

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