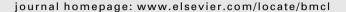


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Bioorganic & Medicinal Chemistry Letters





Bioorganic & Medicinal Chemistry Letters Volume 20, Issue 16, 2010

Contents

BMCL DIGEST

4-Anilino-6-phenyl-quinoline inhibitors of mitogen activated protein kinase-activated protein kinase 2 (MK2)

pp 4738-4740

Henric Olsson, Peter Sjö, Oguz Ersoy, Anna Kristoffersson, Joakim Larsson, Bo Nordén*

2g

Compound 2g was found effective in reducing LPS-induced TNFα production in THP-1 cells, in a manner consistent with MK2 enzyme inhibition.

REGULAR ARTICLES

Synthesis and structure–activity relationship of *N*-(3-azabicyclo[3.1.0]hex-6-ylmethyl)-5-(2-pyridinyl)-1,3-thiazol-2- pp 474 amines derivatives as NPY Y5 antagonists

pp 4741-4744

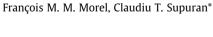
Matteo Biagetti*, Colin Philip Leslie*, Angelica Mazzali, Catia Seri, Domenica Antonia Pizzi, Jonathan Bentley, Thorsten Genski, Romano Di Fabio, Laura Zonzini, Laura Caberlotto

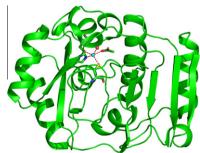
The synthesis and SAR of a series of potent NPY Y5 antagonists (fpKi >9) is reported.

Inhibition of the R1 fragment of the cadmium-containing ζ -class carbonic anhydrase from the diatom *Thalassiosira weissflogii* with anions

pp 4745-4748

Francesca Viparelli, Simona Maria Monti, Giuseppina De Simone, Alessio Innocenti, Andrea Scozzafava, Yan Xu,





A novel series of [3.2.1] azabicyclic biaryl ethers as $\alpha 3\beta 4$ and $\alpha 6/4\beta 4$ nicotinic receptor agonists

pp 4749-4752

John A. Lowe III*, Shari L. DeNinno, Jotham W. Coe, Lei Zhang, Scot Mente, Raymond S. Hurst, Robert J. Mather, Karen M. Ward, Alka Shrikhande, Hans Rollema, David E. Johnson, Weldon Horner, Roxanne Gorczyca, F. David Tingley III, Rouba Kozak, Mark J. Majchrzak, Theresa Tritto, Jen Sadlier, Chris L. Shaffer, Brenda Ellerbrock, Sarah M. Osgood, Mary C. MacDougall, Laura L. McDowell

NHSO
$$_2$$
CH $_3$

17a

 $\alpha 3\beta 4 \text{ K}_i = 0.158 \text{ nM}$
 $\alpha 6/\alpha 4\beta 4 \text{ K}_i = 0.168 \text{ nM}$
 $\alpha 3\beta 4 \text{ EC}_{50} = 3.06 \text{ nM}$
 $\alpha 6/\alpha 4\beta 4 \text{ EC}_{50} = 3.15 \text{ nM}$

We report the discovery of compound 17a, a potent $\alpha 3\beta 4$ and $\alpha 6/4\beta 4$ receptor agonist.



Exploration of a new series of CCR5 antagonists: Multi-dimensional optimization of a sub-series containing N-substituted pyrazoles

pp 4753-4756

Rémy C. Lemoine*, Ann C. Petersen, Lina Setti, Andreas Jekle, Gabrielle Heilek, André deRosier, Changhua Ji, Pamela Berry, David M. Rotstein

Synthesis and cannabinoid-1 receptor binding affinity of conformationally constrained analogs of taranabant

pp 4757-4761

Ihor E. Kopka, Linus S. Lin, James P. Jewell, Thomas J. Lanza, Tung M. Fong, Chun-Pyn Shen, Zhege J. Lao, Sookhee Ha, Laurie G. Castonguay, Lex Van der Ploeg, Mark T. Goulet, William K. Hagmann*

The design, synthesis, and binding activity of ring constrained analogs of the acyclic cannabinoid-1 receptor (CB1R) inverse agonist taranabant 1 are described. The initial inspiration for these taranabant derivatives was its conformation 1a, determined by ¹H NMR, X-ray, and molecular modeling. The constrained analogs were all much less potent than their acyclic parent structure.

Synthesis and pharmacological evaluation of condensed heterocyclic 6-substituted 1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazole and 1,3,4-oxadiazole derivatives of isoniazid

pp 4762-4765

Sadaf J. Gilani*, Suroor A. Khan, Nadeem Siddiqui

Facile and efficient synthesis of condensed heterocyclic 6-substituted 1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazole and 1,3,4-oxadiazole derivatives of isoniazid is reported.

Synthesis of novel oxime-containing pyrazole derivatives and discovery of regulators for apoptosis and autophagy in A549 lung cancer cells

pp 4766-4770

Liang-Wen Zheng, Ying Li, Di Ge, Bao-Xiang Zhao*, Ying-Rui Liu, Hong-Shui Lv, Jun Ding, Jun-Ying Miao*

A series of novel oxime-containing pyrazole derivatives were synthesized and characterized by IR, ¹H NMR, HRMS spectroscopy, and X-ray analysis. A dose-and time-dependent inhibition of proliferation was observed in A549 lung cancer cell after compounds treatment. Hoechst 33258 staining assay and Western blot analysis of LC3-II level showed that the inhibition against A549 cell growth might be attributed to apoptosis and autophagy.



Refinement of the pharmacophore of 3,4-dihydroquinazoline-2(1H)-thiones for their anti-melanogenesis activity

pp 4771-4773

Pillaiyar Thanigaimalai, Vinay K. Sharma, Ki-Cheul Lee, Cheong-Yong Yun, Youngsoo Kim, Sang-Hun Jung*

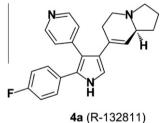
$$H_3C$$
 CH_3
 H_3C
 CH_3
 CH_3



Tetrahydropyridine derivatives with inhibitory activity on the production of proinflammatory cytokines: Part 3

pp 4774-4778

Akira Nakao*, Nobuyuki Ohkawa, Takayoshi Nagasaki, Takashi Kagari, Hiromi Doi, Takaichi Shimozato, Shigeru Ushiyama, Kazumasa Aoki



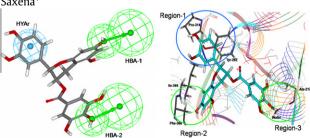
We found that the most promising compound ${\bf 4a}$ (R-132811) in this series inhibits the production of the proinflammatory cytokines in vitro and in vivo (e.g., TNF α IC $_{50}$ = 0.026 μ M, TNF α ID $_{50}$ = 0.93 mg/kg).



Integrated ligand and structure based studies of flavonoids as fatty acid biosynthesis inhibitors of *Plasmodium falciparum*

pp 4779-4781

Amit K. Gupta, Shruti Saxena, Mridula Saxena*



A common feature pharmacophore with two hydrogen-bond acceptor and one aromatic hydrophobic feature has been generated using seven active flavonoids. Docking studies of these compounds well corroborates with the pharmacophore model. Therefore model could be useful for identification of potential novel FAS-II inhibitors.

Inhibitors of osteoclastogenesis from Lawsonia inermis leaves

pp 4782-4784

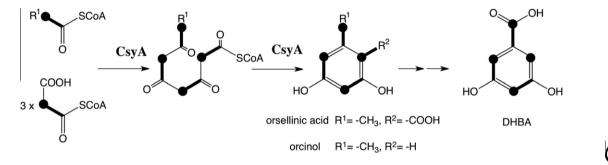
Nguyen Xuan Cuong, Nguyen Xuan Nhiem, Nguyen Phuong Thao, Nguyen Hoai Nam, Nguyen Tien Dat, Hoang Le Tuan Anh, Le Mai Huong, Phan Van Kiem*, Chau Van Minh, Ji-Hee Won, Won-Yoon Chung, Young Ho Kim*

Ten phenolic compounds (1-10) were isolated from a methanol extract of Lawsonia inermis leaves including two new ones, lawsoniasides A (1) and B (2). Compounds 4 and 5 showed a significant inhibition on receptor activator for nuclear factor-kB ligand-induced osteoclast formation in murine bone-marrow macrophages.

Aspergillus oryzae type III polyketide synthase CsyA is involved in the biosynthesis of 3,5-dihydroxybenzoic acid

pp 4785-4788

Yasuyo Seshime, Praveen Rao Juvvadi, Katsuhiko Kitamoto, Yutaka Ebizuka, Takamasa Nonaka, Isao Fujii*



Improving the permeability of the hydroxyethylamine BACE-1 inhibitors: Structure-activity relationship of P2' substituents

pp 4789-4794

Anh P. Truong, Gary D. Probst*, Jose Aquino, Larry Fang, Louis Brogley, Jennifer M. Sealy, Roy K. Hom*, John A. Tucker, Varghese John, Jay S. Tung, Michael A. Pleiss, Andrei W. Konradi, Hing L. Sham, Michael S. Dappen, Gergley Tóth, Nanhua Yao, Eric Brecht, Hu Pan, Dean R. Artis, Lany Ruslim, Michael P. Bova, Sukanto Sinha, Ted A. Yednock, Wes Zmolek, Kevin P. Quinn, John-Michael Sauer

Herein, we describe further evolution of hydroxyethylamine inhibitors of BACE-1 with enhanced permeability characteristics necessary for CNS penetration. Variation at the P2' position of the inhibitor with more polar substituents led to compounds 19 and 32, which retained the potency of more lipophilic analog 1 but with much higher observed passive permeability in MDCK cellular assay.



Discovery and optimization of N-acyl and N-aroylpyrazolines as B-Raf kinase inhibitors

pp 4795-4799

Christopher Blackburn*, Matthew O. Duffey, Alexandra E. Gould, Bheemashankar Kulkarni, Iane X. Liu, Saurabh Menon, Masayuki Nagayoshi, Tricia J. Vos, Juliet Williams

A high throughput screen identified N-aroylpyrazoline 1 as a selective inhibitor of the V600E mutant of B-Raf kinase. Parallel synthesis of acyl, aroyl, and sulfonyl derivatives led to the identification of several potent inhibitors in both enzymatic and cellular (pERK) assays such as compound 42.

A375 pERK IC₅₀: 1,800 nM

V600E B-Raf IC₅₀: 19 nM A375 pERK IC₅₀: 180 nM

Discovery and optimization of pyrazoline compounds as B-Raf inhibitors

pp 4800-4804

Matthew O. Duffey*, Ruth Adams, Christopher Blackburn, Ryan W. Chau, Susan Chen, Katherine M. Galvin, Khristofer Garcia, Alexandra E. Gould, Paul D. Greenspan, Sean Harrison, Shih-Chung Huang, Mi-Sook Kim, Bheemashankar Kulkarni, Steven Langston, Jane X. Liu, Li-Ting Ma, Saurabh Menon, Masayuki Nagayoshi,

R. Scott Rowland, Tricia J. Vos, Tianlin Xu, Johnny J. Yang, Shaoxia Yu, Qin Zhang

V600E B-Raf IC₅₀: 200 nM A375 pERK IC₅₀: 1,800 nM

V600E B-Raf IC₅₀: 3 nM pERK IC₅₀: 18 nM

A DOTA-peptide conjugate by copper-free click chemistry

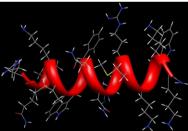
pp 4805-4807

Molly E. Martin, Sharavathi G. Parameswarappa, M. Sue O'Dorisio, F. Christopher Pigge*, Michael K. Schultz*

New antifungal peptides. Synthesis, bioassays and initial structure prediction by CD spectroscopy

pp 4808-4811

Mónica S. Olivella, Ana M. Rodríguez, Susana A. Zacchino, Csaba Somlai, Botond Penke, Victor Farkas, András Perczel, Ricardo D. Enriz*



We report the synthesis, the conformational study by using CD spectroscopy and the antifungal assays of penetratin analogues. These peptides displayed a significant antifungal activity against Candida albicans and Cryptococcus neoformans.



Structure and activity relationships of tartrate-based TACE inhibitors

pp 4812-4815

Dansu Li*, Janeta Popovici-Muller, David B. Belanger, John Caldwell, Chaoyang Dai, Maria David, Vinay M. Girijavallabhan, Brian J. Lavey, Joe F. Lee, Zhidan Liu, Rob Mazzola, Razia Rizvi, Kristin E. Rosner, Bandarpalle Shankar, Jim Spitler, Pauline C. Ting, Henry Vaccaro, Wensheng Yu, Guowei Zhou, Zhaoning Zhu, Xiaoda Niu, Jing Sun, Zhuyan Guo, Peter Orth, Shiying Chen, Joseph A. Kozlowski, Daniel J. Lundell, Vincent Madison, Brian McKittrick, John J. Piwinski, Neng-Yang Shih, Gerald W. Shipps Jr., M. Arshad Siddiqui, Corey O. Strickland

$1-Methyl-1 \\ H-pyrrole-2-carbonitrile\ containing\ tetrahydron aphthalene\ derivatives\ as\ non-steroidal\ progesterone\ receptor\ antagonists$

pp 4816-4818

Jeffrey C. Kern*, Eugene Terefenko, Eugene Trybulski, Thomas J. Berrodin, Jeffrey Cohen, Richard C. Winneker, Matthew R. Yudt, Zhiming Zhang, Yuan Zhu, Puwen Zhang

Progesterone receptor antagonists with low nanomolar in vitro potency are reported.

Optimization of α -ketoamide based p38 inhibitors through modifications to the region that binds to the allosteric site

pp 4819-4824

Antonio Garrido Montalban*, Erik Boman, Chau-Dung Chang, Susana Conde Ceide, Russell Dahl, David Dalesandro, Nancy G. J. Delaet, Eric Erb, Justin T. Ernst, Andrew Gibbs, Jeffrey Kahl, Linda Kessler, Jeff Kucharski, Christopher Lum, Jan Lundström, Stephen Miller, Hiroshi Nakanishi, Edward Roberts, Eddine Saiah, Robert Sullivan, Jan Urban, Zhijun Wang, Christopher J. Larson

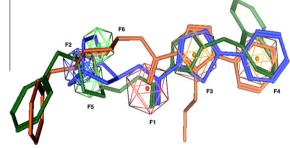
The design and synthesis of novel α-ketoamide based p38 inhibitors is reported.

Discovery of novel $\alpha 7$ nicotinic receptor antagonists

pp 4825-4830

Youyi Peng, Qiang Zhang, Gretchen L. Snyder, Hongwen Zhu, Wei Yao, John Tomesch, Roger L. Papke, James P. O'Callaghan, William J. Welsh, Lawrence P. Wennogle*

Two distinct families of small molecules were discovered as novel selective $\alpha 7$ nicotinic acetylcholine receptor (nAChR) antagonists by pharmacophore-based virtual screening. These antagonists exhibited good brain penetration and neuroprotection in a mouse seizure-like behavior model induced by the nerve agent diisopropylfluorophosphate (DFP).



$Anti-T.\ cruzi\ activities\ and\ QSAR\ studies\ of\ 3-arylquinoxaline-2-carbonitrile\ di-N-oxides$

pp 4831-4835

Esther Vicente*, Pablo R. Duchowicz, Diego Benítez, Eduardo A. Castro, Hugo Cerecetto, Mercedes González, Antonio Monge

21, IC₅₀=7.1 μM

(Nfx, IC₅₀=7.7 μ M)

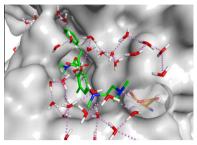
In vitro anti-Trypanosoma cruzi activity and QSAR studies of 3-arylquinoxaline-2-carbonitrile di-N-oxides is reported, emerging as new anti-trypanosomal agents. In addition, a rational guide for the proposal of new candidate structures is achieved.



Improvement of both plasmepsin inhibitory activity and antimalarial activity by 2-aminoethylamino substitution

pp 4836-4839

Takuya Miura, Koushi Hidaka, Tsuyoshi Uemura, Keisuke Kashimoto, Yuto Hori, Yuko Kawasaki, Adam J. Ruben, Ernesto Freire, Tooru Kimura, Yoshiaki Kiso*



Attachments of 2-aminoethylamino substituents to an allophenylnorstatine-containing plasmepsin inhibitor enhanced both plasmepsin inhibitory and antimalarial activities.

Fluorine-18 labeled galactosylated chitosan for asialoglycoprotein-receptor-mediated hepatocyte imaging

pp 4840-4844

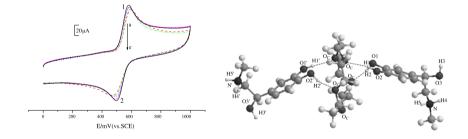
Wenjiang Yang, Tiantian Mou, Wenyan Guo, Huihui Jing, Cheng Peng, Xianzhong Zhang*, Yunchuan Ma, Boli Liu*

Chitosan based novel ASGP imaging agent [18F]FB-GC was synthesized and evaluated in mice.

Experimental and theoretical study on the supramolecular complexes of 15-crown-5 with adrenaline

pp 4845-4849

Tao Liu, Zhang-Yu Yu*



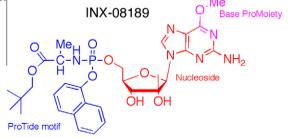


Design, synthesis and evaluation of a novel double pro-drug: INX-08189. A new clinical candidate for hepatitis C virus

pp 4850-4854

Christopher McGuigan*, Karolina Madela, Mohamed Aljarah, Arnaud Gilles, Andrea Brancale, Nicola Zonta, Stanley Chamberlain, John Vernachio, Jeff Hutchins, Andrea Hall, Brenda Ames, Elena Gorovits, Babita Ganguly, Alexander Kolykhalov, Jin Wang, Jerry Muhammad, Joseph M. Patti, Geoffrey Henson

Phosphoramidate ProTides of 2'-C-Me-6-MeOG are up to 500-fold more potent versus HCV than the 2'-C-MeG parent, being active at nanomolar levels. The lead has entered phase 1 clinical trials for HCV.



Morroniside cinnamic acid conjugate as an anti-inflammatory agent

pp 4855-4857

Yoshinori Takeda, Naomi Tanigawa, Fortunatus Sunghwa, Masayuki Ninomiya, Makoto Hagiwara, Kenji Matsushita, Mamoru Koketsu*

Synthesis of potent chemical inhibitors of dynamin GTPase

pp 4858-4864

Suho Lee, Kwan-Young Jung, Joohyun Park, Joong-Heui Cho, Yong-Chul Kim, Sunghoe Chang*

The synthesis of the potent dynamin GTPase inhibitors (IC₅₀ = 5.1 μ M for DD-6; 3.6 μ M for DD-11) is reported.



Synthesis and anti-cancer activity of chalcone linked imidazolones

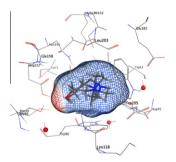
pp 4865-4869

Ahmed Kamal*, G. Ramakrishna, P. Raju, A. Viswanath, M. Janaki Ramaiah, G. Balakishan, Manika Pal-Bhadra*



3-D-QSAR and docking studies on the neuronal choline transporter

Werner J. Geldenhuys*, David D. Allen, Paul R. Lockman





pp 4870-4877

Identification of N-(2-(azepan-1-yl)-2-phenylethyl)-benzenesulfonamides as novel inhibitors of GlyT1

pp 4878-4881

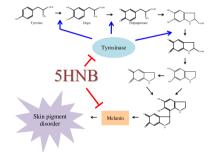
Jeffrey G. Varnes, Janet M. Forst, Tiffany N. Hoerter, Christopher R. Holmquist, Deidre E. Wilkins, Gaochao Tian, Gerald Jonak, Xia Wang, William M. Potts, Michael W. Wood, Cristóbal Alhambra, Todd A. Brugel, Jeffrey S. Albert*

A series of novel GlyT1 inhibitors is described.

A newly synthesized, potent tyrosinase inhibitor: 5-(6-Hydroxy-2-naphthyl)-1,2,3-benzenetriol

pp 4882-4884

Jehun Choi, Sung Jin Bae, Young Mi Ha, Jae Kyung No, Eun Kyeong Lee, Jun Sik Lee, Suhee Song, Hyojin Lee, Hongsuk Suh, Byung Pal Yu, Hae Young Chung*





Enhanced selectivity profile of pyrazole-urea based DFG-out $p38\alpha$ inhibitors

pp 4885-4891

Hu Liu*, Cyrille Kuhn, Frederic Feru, Suzanne L. Jacques, Gayatri D. Deshmukh, Ping Ye, Glen R. Rennie, Theresa Johnson, Steven Kazmirski, Simon Low, Rocco Coli, Yuan-hua Ding, Alan C. Cheng, Haile Tecle, Jessie M. English, Robert Stanton, Joe C. Wu*

The development of potent and selective p38 inhibitor 11 is reported.

Synthesis and vasodilative activity of tanshinone IIA derivatives

pp 4892-4894

Yue-Feng Bi, Hai-Wei Xu, Xiao-Qing Liu, Xiao-Juan Zhang, Zhen-Ji Wang, Hong-Min Liu*

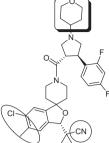
Vasodilation activity in vitro of them was valuated on the contractile response of vascular thoracic aorta smooth muscle from Wistar rats for the first time. Most of them exhibited a concentration-dependent inhibition of the contractile response of norepinephrine.

Discovery of potent, selective, and orally bioavailable 3*H*-spiro[isobenzofuran-1,4'-piperidine] based melanocortin subtype-4 receptor agonists

pp 4895-4900

Liangqin Guo*, Zhixiong Ye, Jian Liu, Shuwen He, Raman K. Bakshi, Iyassu K. Sebhat, Peter H. Dobbelaar, Qingmei Hong, Tianying Jian, James P. Dellureficio, Nancy N. Tsou, Richard G. Ball, David H. Weinberg, Tanya MacNeil, Rui Tang, Constantin Tamvakopoulos, Qianping Peng, Howard Y. Chen, Airu S. Chen, William J. Martin, D. Euan MacIntyre, Alison M. Strack, Tung M. Fong, Matthew J. Wyvratt, Ravi P. Nargund

Design, synthesis, structure–activity relationship, and in vivo pharmacological data of a series of 3*H*-spiro[isobenzofuran-1,4'-piperidine] based compounds as potent, selective, orally bioavailable and brain penetrable melanocortin subtype-4 receptor (MC4R) agonists are disclosed.

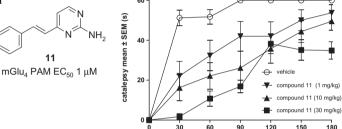


An orally bioavailable positive allosteric modulator of the $mGlu_4$ receptor with efficacy in an animal model of motor dysfunction

pp 4901-4905

Stephen P. East*, Samantha Bamford, Matthias G. A. Dietz, Christian Eickmeier, Adam Flegg, Boris Ferger, Mark J. Gemkow, Ralf Heilker, Bastian Hengerer, Adrian Kotey, Pui Loke, Gerhard Schänzle, Hans-Dieter Schubert, John Scott, Mark Whittaker, Mildred Williams, Przemyslaw Zawadzki, Kai Gerlacíi*

A high-throughput screening campaign identified 4-((*E*)-styryl)-pyrimidin-2-ylamine (11) as a positive allosteric modulator of the metabotropic glutamate (mGlu) receptor subtype 4. An evaluation of the structure-activity relationships (SAR) of 11 is described and the efficacy of this compound in a haloperidol-induced catalepsy rat model following oral administration is presented.

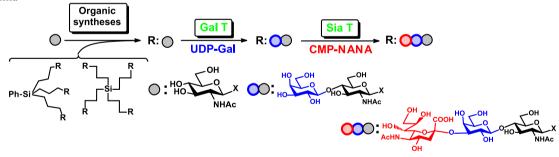


Synthesis of sialyllactosamine clusters using carbosilane as core scaffolds by means of chemical and enzymatic approaches

pp 4906-4910

time after haloperidol (min)

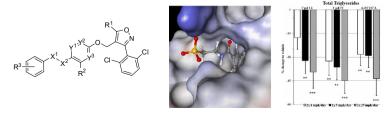
Koji Matsuoka*, Reina Kaneko, Tetsuo Koyama, XiaoTao Ma, Yasuaki Esumi, Takemichi Nakamura, Ken Hatano, Daiyo Terunuma



Synthesis and pharmacological validation of a novel series of non-steroidal FXR agonists

pp 4911-4917

Ulrich Abel, Thomas Schlüter, Andreas Schulz, Eva Hambruch, Christoph Steeneck, Martin Hornberger, Thomas Hoffmann, Sanja Perović-Ottstadt, Olaf Kinzel, Michael Burnet, Ulrich Deuschle, Claus Kremoser*



To overcome the known liabilities of GW4064 a series of analogues were synthesized with increased potency in vitro and with superior lipid lowering effects in db/db mice compared to 6-ethyl-CDCA.



Design, synthesis, and structure—activity relationship study of conformationally constrained analogs of indole-3-carboxamides as novel CB1 cannabinoid receptor agonists

pp 4918-4921

Takao Kiyoi, Mark York, Stuart Francis, Darren Edwards, Glenn Walker, Andrea K. Houghton, Jean E. Cottney, James Baker, Julia M. Adam*

$$\begin{array}{c} O \\ N \\ N \\ N \\ N \\ N \\ N \\ X = O \text{ or } CH_2 \\ \end{array}$$

Constrained analogs

Synthesis, selective anti-*Helicobacter pylori* activity, and cytotoxicity of novel N-substituted-2-oxo-2*H*-1-benzopyran-3-carboxamides

pp 4922-4926

Franco Chimenti, Bruna Bizzarri*, Adriana Bolasco, Daniela Secci, Paola Chimenti, Arianna Granese, Simone Carradori, Daniela Rivanera, Alessandra Zicari, M. Maddalena Scaltrito, Francesca Sisto

A novel class of 20 N-substituted-3-carboxamido-coumarin derivatives were prepared and evaluated for their selective anti-Helicobacter pylori activity against several isolates of clinical strains, including five metronidazole resistant ones. Furthermore, a cytotoxic screening was carried out on the most active derivatives.

Structure–activity relationship of lupane-triterpene glycosides from Acanthopanax koreanum on spleen lymphocyte IL-2 and IFN- γ

pp 4927-4931

Nguyen Xuan Nhiem, Phan Van Kiem, Chau Van Minh, Bui Huu Tai, Nguyen Huu Tung, Do Thi Ha, Kwang Su Soung, Jun Ho Kim, Ji Young Ahn, Young-Mi Lee, Young Ho Kim*

Phytochemical investigation resulted in isolation of three new lupane-triterpene glycosides acankoreosides M–O (1, 2 and 8) from the leaves of *Acanthopanax koreanum* (Araliaceae). Compounds 4, 5, 7, and 11 (5, 25, and 100 μ M) significantly increased IFN- γ and IL-2 release in spleen cells.

Smoothened antagonists for hair inhibition

pp 4932-4935

Jie Jack Li*, Veerabahu Shanmugasundaram, Satya Reddy, Laura L. Fleischer, Zenquan Wang, Yvonne Smith, William G. Harter, Wen-Song Yue, Manju Swaroop, Ling Li, Christy Xiaodong Ji, Danielle Dettling, Bella Osak, Laura R. Fitzgerald, Robert Conradi

A series of aminomethylpyrazoles were prepared and evaluated using cell-based Smoothened β -lactamase reporter assay and Smoothened binding assay. Potent Smoothened antagonists **10k** and **10l** were found to inhibit hair growth in vivo in the C3H/HeN mouse hair growth model. The more selective compound **10l** was tested negative in the 3T3 NRU assay, indicating a low risk for causing photo-irritation and was efficacious using the C3H/HeN mouse hair growth model although it was slightly less efficacious than that of the reference compound effornithine (**7**).

SMOTT, IC $_{50}$ = 8.27 nM SMOTT, IC $_{50}$ = 124 nM MED = 3% C3H/HeN mouse

A mechanism based protein crosslinker for acyl carrier protein dehydratases

pp 4936-4939

Jordan L. Meier, Robert W. Haushalter, Michael D. Burkart*

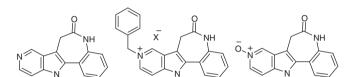
A chemoenzymatic method for the crosslinking of protein partners of the fatty acid biosynthetic pathway is detailed.



pp 4940-4944

Concise synthesis and CDK/GSK inhibitory activity of the missing 9-azapaullones

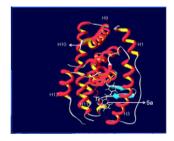
David P. Power, Olivier Lozach, Laurent Meijer*, David H. Grayson*, Stephen J. Connon*



Synthesis and docking studies on styryl chromones exhibiting cytotoxicity in human breast cancer cell line

pp 4945-4950

Seema Bhatnagar*, Shakti Sahi, Puneet Kackar, Swati Kaushik, Manan K. Dave, Akshara Shukla, Ashita Goel



Three dimensional structure of ER β docked with compound **5a** using Maestro.Beta sheet has been shown in blue color and compound has been shown as ball and stick model.



Synthesis and biological activity of a series of tetrasubstituted-imidazoles as P2X7 antagonists

pp 4951-4954

Robert J. Gleave*, Daryl S. Walter, Paul J. Beswick, Elena Fonfria, Anton D. Michel, Shilina A. Roman, Sac-Pham Tang

hP2X₇ pIC₅₀ 7.4

pe1

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Corrigendum @

Erratum pp 4955–4959

*Corresponding author

(i) Supplementary data available via ScienceDirect

@ This article does not appear in the printed issue, it is available in the online version of this issue.

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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ISSN 0960-894X