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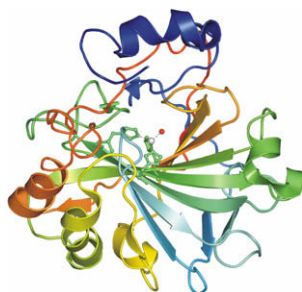
Contents

BMCL DIGEST

Carbonic anhydrase inhibitors

Claudiu T. Supuran*

pp 3467–3474



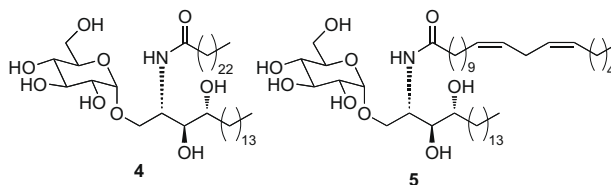
CA II protein fold, Zn(II) ion, and its coordination by three histidine residues.

REGULAR ARTICLES

Synthesis and biological activity of α -glucosyl C24:0 and C20:2 ceramides

Peter J. Jarvis, Natacha Veerapen, Gabriel Bricard, Liam R. Cox, Steven A. Porcelli, Gurdial S. Besra*

pp 3475–3478



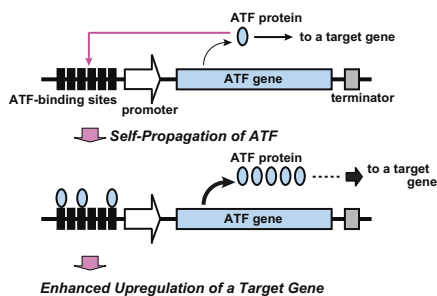
α -Glucosyl ceramides **4** and **5** have been synthesised and their ability to stimulate the activation and expansion of iNKT cells evaluated.



Self-propagating artificial transcription factors to enhance upregulation of target genes

Tomoaki Mori, Jun Sasaki, Yoshiaki Saito, Yasuhiro Aoyama, Takashi Sera*

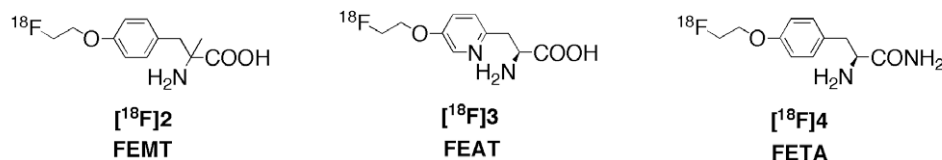
pp 3479–3481



Synthesis and in vitro evaluation of ^{18}F labeled tyrosine derivatives as potential Positron Emission Tomography (PET) imaging agents

pp 3482–3485

Limin Wang, Wenchao Qu, Brian Lieberman, Karl Ploessl, Hank F. Kung*

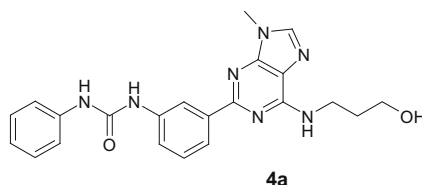


Synthesis and in vitro evaluation of three new fluoroalkyl tyrosine derivatives as PET imaging agents are reported.

Towards Gram-positive antivirulence drugs: New inhibitors of *Streptococcus agalactiae* Stk1

pp 3486–3490

Mayalen Oxoby, François Moreau, Lionel Durant, Alexis Denis, Jean-Marie Genevard, Vanida Vongsouthi, Sonia Escaich, Vincent Gerusz*

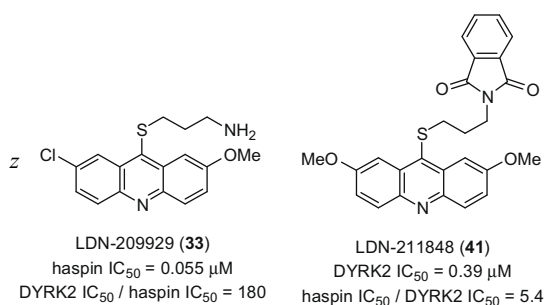


A structure–activity relationship study of a screening hit has led to the identification of bisaryleureas as potent inhibitors of *Streptococcus agalactiae* Stk1. As this target has been directly linked to bacterial virulence, these inhibitors can be considered as a promising step towards antivirulence drugs.

Structure–activity relationship study of acridine analogs as haspin and DYRK2 kinase inhibitors

pp 3491–3494

Gregory D. Cuny*, Maxime Robin, Natalia P. Ulyanova, Debasis Patnaik, Valerie Pique, Gilles Casano, Ji-Feng Liu, Xiangjie Lin, Jun Xian, Marcie A. Glicksman, Ross L. Stein, Jonathan M. G. Higgins

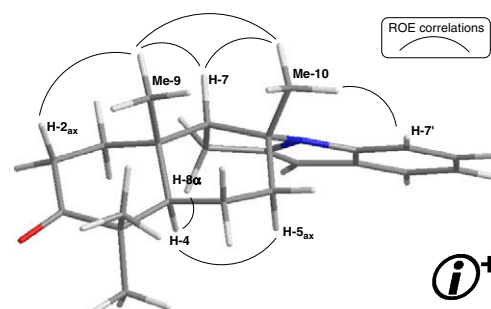


Antitrypanosomal alkaloids from *Polyalthia suaveolens* (Annonaceae): Their effects on three selected glycolytic enzymes of *Trypanosoma brucei*

pp 3495–3498

Igor Ngantchou*, Barthélemy Nyasse**, Colette Denier, Casimir Blonski, Véronique Hannaert, Bernd Schneider

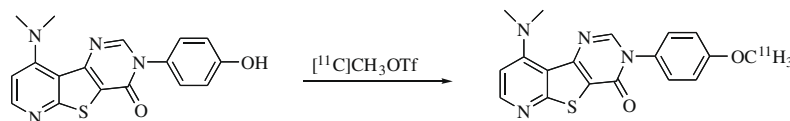
In continuation of our study on medicinal plants of Cameroon, stem barks of *Polyalthia suaveolens* were phytochemically studied. This investigation yielded a new indolosesquiterpene alkaloid, named polysin (**1**) and four hitherto known alkaloids (**2–5**). Polysin (**1**) appeared as a competitive reversible inhibitor (K_i = 10 μM) of phosphofructo kinase (PFK) of *Trypanosoma brucei* with respect to fructose-6-phosphate (K_i/K_M = 0.05) and could be used in the design of new trypanocidal drugs. The other isolated compounds (**2–5**) also exhibited interesting inhibitory effects on selected glycolytic enzymes (PFK, glyceraldehyde-3-phosphate dehydrogenase and aldolase).



Synthesis, in vitro and in vivo evaluation of [¹¹C]MMTP: A potential PET ligand for mGluR1 receptors

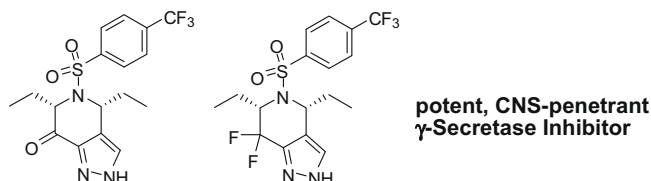
pp 3499–3501

Jaya Prabhakaran, Vattoly J. Majo, Matthew S. Milak, Suham A. Kassir, Mikael Palner, Lyudmila Savenkova, Pratap Mali, Victoria Arango, J. John Mann, Ramin V. Parsey, J.S. Dileep Kumar*

**Discovery of a novel sulfonamide-pyrazolopiperidine series as potent and efficacious γ -secretase inhibitors (Part II)**

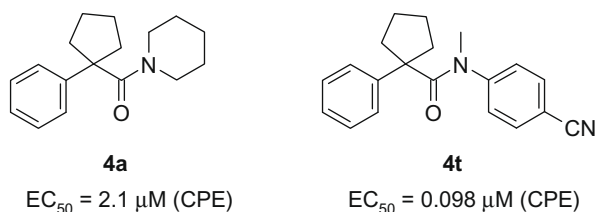
pp 3502–3506

Xiacong M. Ye*, Andrei W. Konradi, Jenifer Smith, Danielle L. Aubele, Albert W. Garofalo, Jennifer Marugg, Marty L. Neitzel, Chris M. Semko, Hing L. Sham, Minghua Sun, Anh P. Truong, Jing Wu, Hongbin Zhang, Erich Goldbach, John-Michael Sauer, Elizabeth F. Bringham, Michael Bova, Guriqbal S. Basi

**Discovery of novel 1-phenyl-cycloalkane carbamides as potent and selective influenza fusion inhibitors**

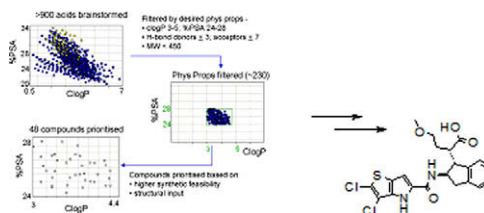
pp 3507–3510

Guozhi Tang*, Zongxing Qiu, Xianfeng Lin, Wentao Li, Lei Zhu, Shaohua Li, Haodong Li, Lisha Wang, Li Chen, Jim Z. Wu, Wengang Yang

**Discovery of a series of indan carboxylic acid glycogen phosphorylase inhibitors**

pp 3511–3514

Stuart N. L. Bennett, Andrew D. Campbell, Andrew Hancock, Craig Johnstone, Peter W. Kenny, Adrian Pickup, Alleyn T. Plowright*, Nidhal Selmi, Iain Simpson, Andy Stocker, David P. Whalley, Paul R. O. Whittamore

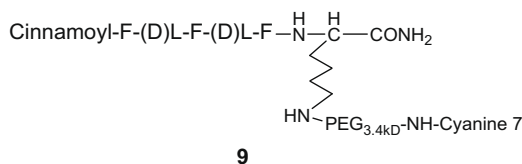


A series of carboxylic acid glycogen phosphorylase inhibitors, which have potential as oral antidiabetic agents, is described. Defining and applying simple physicochemical design criteria was used to assess the opportunity and to focus synthetic efforts on compounds with the greatest probability of success. The study led to compound **17**, which exhibits a good balance of properties including potent inhibition of recombinant human liver glycogen phosphorylase in vitro, a good DMPK profile including excellent bioavailability and low clearance and good in vivo activity in a glucagon challenge model of diabetes in Zucker rats.

Synthesis of the Cyanine 7 labeled neutrophil-specific agents for noninvasive near infrared fluorescence imaging

pp 3515–3517

Li Xiao, Yi Zhang, Zhongqiu Liu, Min Yang, Lin Pu, Dongfeng Pan*



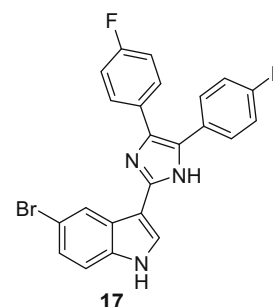
A series of Cyanine 7 labeled neutrophil-specific agents were developed for noninvasive near infrared fluorescence imaging.

Potent antimicrobial activity of 3-(4,5-diaryl-1H-imidazol-2-yl)-1H-indole derivatives against methicillin-resistant *Staphylococcus aureus*

pp 3518–3520

Raed A. Al-Qawasmeh, Mario Huesca*, Venkata Nedunuri, Robert Peralta, Jim Wright, Yoon Lee, Aiping Young

Compound **17** [3-(4,5-bis(4-fluorophenyl)-1H-imidazol-2-yl)-5-bromo-1H-indole] was identified as a potent antimicrobial derivative with MIC of 1 µg/mL against methicillin-resistant *Staphylococcus aureus*.

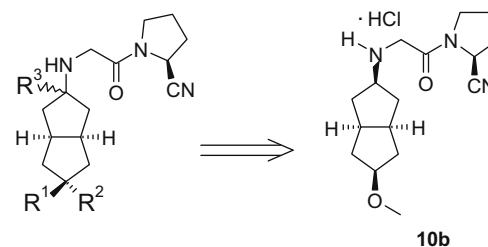


Synthesis and biological evaluation of bicyclo[3.3.0]octane derivatives as dipeptidyl peptidase 4 inhibitors for the treatment of type 2 diabetes

pp 3521–3525

Tang Peng Cho*, Lin Zhi Gang, Yang Fang Long, Wang Yang, Wang Qian, Zhang Lei, Luo Jing Jing, Feng Ying, Yan Pang Ke, Leng Ying, Feng Jun

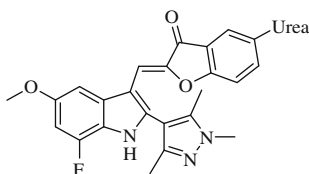
A series of novel bicyclo[3.3.0]octane derivatives have been synthesized and found to be dipeptidyl peptidase 4 (DPP-4) inhibitors. Compounds **10a** and **10b** demonstrate good efficacies in oral glucose tolerance tests.



5-Ureidobenzofuranone indoles as potent and efficacious inhibitors of PI3 kinase-α and mTOR for the treatment of breast cancer

pp 3526–3529

Nan Zhang*, Semiramis Ayral-Kaloustian*, James T. Anderson, Thai Nguyen, Sasmita Das, Aranapakam M. Venkatesan, Natasja Brooijmans, Judy Lucas, Ker Yu, Irwin Hollander, Robert Mallon



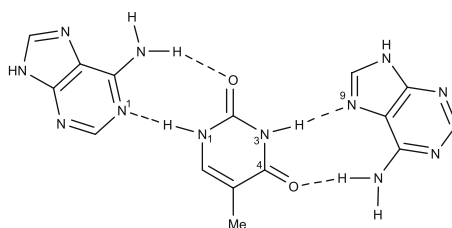
A series of 5-ureidobenzofuran-3-one indoles as potent inhibitors of PI3K-α and mTOR has been developed. In the MDA-MB-361 breast cancer model, the lead compound shrank the tumor size remarkably when dosed at 25 mg/kg iv on days 1, 5, and 9.



Crystal structure of an intermolecular 2:1 complex between adenine and thymine. Evidence for both Hoogsteen and 'quasi-Watson-Crick' interactions

pp 3530–3533

Sosale Chandrasekhar*, Tangali R. Ravikumar Naik, Susanta K. Nayak, Tayur N. Guru Row*

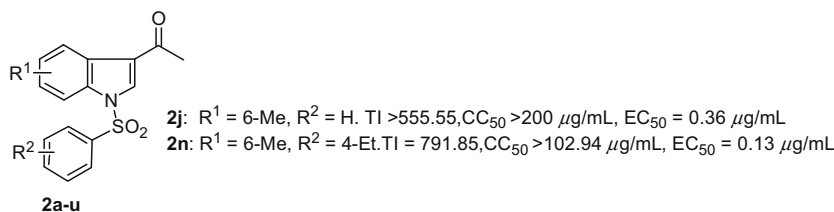


The first known complex of the titled DNA bases was prepared by co-crystallization and studied by X-ray diffraction.

Anti HIV-1 agents 5: Synthesis and anti-HIV-1 activity of some *N*-arylsulfonyl-3-acetylindoles in vitro

pp 3534–3536

Jun-Qiang Ran, Ning Huang, Hui Xu*, Liu-Meng Yang, Min Lv*, Yong-Tang Zheng*

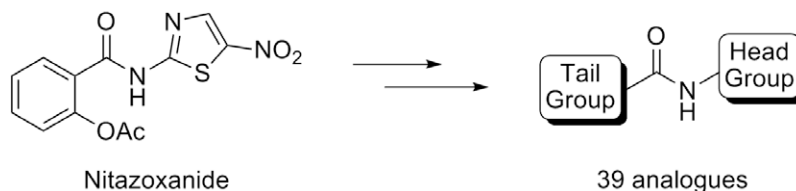


It demonstrated that introduction of the acetyl group at the 3-position of *N*-arylsulfonyl-6-methylindoles could generally lead to the more potent analogs.

**Biological activity of modified and exchanged 2-amino-5-nitrothiazole amide analogues of nitazoxanide**

pp 3537–3539

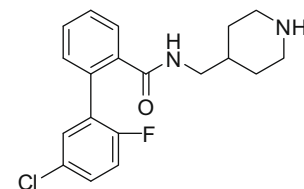
T. Eric Ballard*, Xia Wang, Igor Olekhovich, Taylor Koerner, Craig Seymour, Paul S. Hoffman, Timothy L. Macdonald

**2' Biaryl amides as novel and subtype selective M_1 agonists. Part I: Identification, synthesis, and initial SAR**

pp 3540–3544

Brian Budzik*, Vincenzo Garzya*, Dongchuan Shi, James J. Foley, Ralph A. Rivero, Christopher J. Langmead, Jeannette Watson, Zining Wu, Ian T. Forbes, Jian Jin*

Biaryl amides were discovered as novel and subtype selective M_1 agonists. The identification, synthesis, and initial SAR that led to the discovery of compound **3j** are described.



3j, M_1 $\text{pEC}_{50} = 8.0$
 > 100-fold selective over $M_2 - M_5$

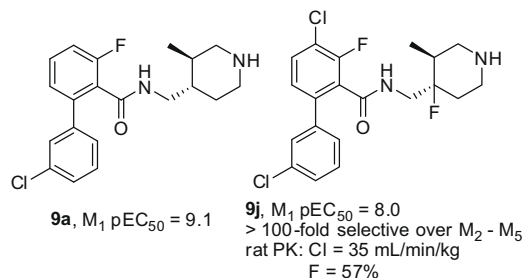


2' Biaryl amides as novel and subtype selective M₁ agonists. Part II: Further optimization and profiling

pp 3545–3549

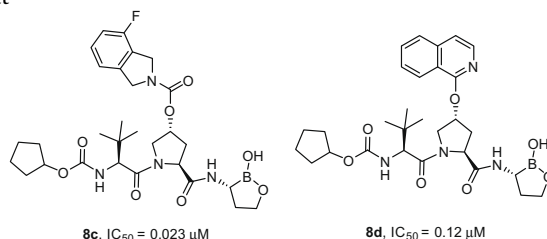
Brian Budzik*, Vincenzo Garzya*, Dongchuan Shi, Graham Walker, Yann Lauchart, Adam J. Lucas, Ralph A. Rivero, Christopher J. Langmead, Jeannette Watson, Zining Wu, Ian T. Forbes, Jian Jin*

Optimization and further SAR exploration of the biaryl amide series resulted in the discovery of orally bioavailable, CNS-penetrant M₁ agonists with excellent potency and subtype selectivity.

**Synthesis and evaluation of novel α -amino cyclic boronates as inhibitors of HCV NS3 protease**

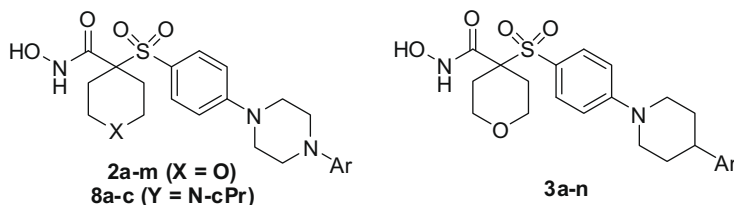
pp 3550–3556

Xianfeng Li*, Yong-Kang Zhang, Yang Liu, Charles Z. Ding, Qun Li, Yasheen Zhou, Jacob J. Plattner, Stephen J. Baker, Xuelei Qian, Dazhong Fan, Liang Liao, Zhi-Jie Ni, Gemma V. White, Jackie E. Mordaunt, Linos X. Lazarides, Martin J. Slater, Richard L. Jarvest, Pia Thommes, Malcolm Ellis, Colin M. Edge, Julia A. Hubbard, Don Somers, Paul Rowland, Pamela Nassau, Bill McDowell, Tadeusz J. Skarzynski, Wieslaw M. Kazmierski*, Richard M. Grimes, Lois L. Wright, Gary K. Smith, Wuxin Zou, Jon Wright, Lewis E. Pennicott

**Orally bioavailable dual MMP-1/MMP-14 sparing, MMP-13 selective α -sulfone hydroxamates**

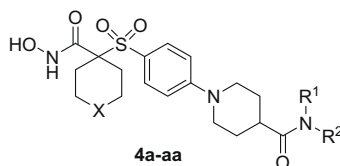
pp 3557–3560

Stephen A. Kolodziej, Susan L. Hockerman, Terri L. Boehm, Jeffery N. Carroll, Gary A. DeCrescenzo, Joseph J. McDonald, Debbie A. Mischke, Grace E. Munie, Theresa R. Fletcher, Joseph G. Rico, Nathan W. Stehle, Craig Swearingen, Daniel P. Becker*

**MMP-13 selective isonipecotamide α -sulfone hydroxamates**

pp 3561–3564

Stephen A. Kolodziej, Susan L. Hockerman, Gary A. DeCrescenzo, Joseph J. McDonald, Debbie A. Mischke, Grace E. Munie, Theresa R. Fletcher, Nathan Stehle, Craig Swearingen, Daniel P. Becker*



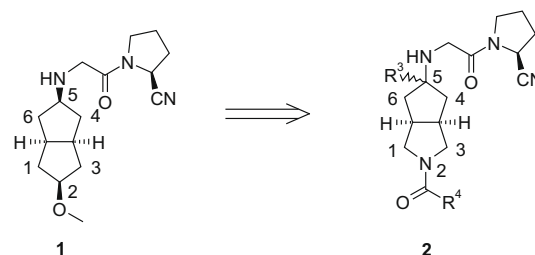
N-Aryl isonipecotamide α -sulfone hydroxamates have been prepared utilizing a combination of solution-phase and resin-bound library technologies to afford compounds that are potent and highly selective for MMP-13.

Synthesis and biological evaluation of azobicyclo[3.3.0] octane derivatives as dipeptidyl peptidase 4 inhibitors for the treatment of type 2 diabetes

pp 3565–3568

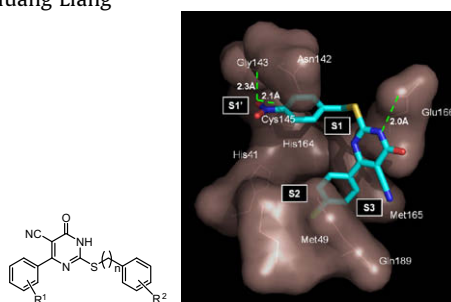
Tang Peng Cho*, Yang Fang Long, Lin Zhi Gang, Wang Yang, Lu He Jun, Shen Guang Yuan, Fu Jian Hong, Wang Lin, Guan Dong Liang, Zhang Lei, Luo Jing Jing, Gong Ai Shen, She Gao Hong, Wang Dan, Feng Ying, Yan Pang Ke, Leng Ying, Feng Jun, Mong Xian Tai

A series of novel azobicyclo[3.3.0]octane derivatives were synthesized and evaluated as dipeptidyl peptidase 4 (DPP-4) inhibitors. The effort resulted in the discovery of inhibitor **2a**, which exhibited excellent efficacies in an oral glucose tolerance test. Introduction of methyl group (**2j**) could prolong the inhibition of serum DPP-4 activity.

**Synthesis, docking studies, and evaluation of pyrimidines as inhibitors of SARS-CoV 3CL protease**

pp 3569–3572

R. Ramajayam, Kian-Pin Tan, Hun-Ge Liu, Po-Huang Liang*

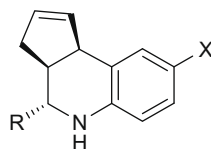


2-(Benzylthio)-6-oxo-4-phenyl-1,6-dihydropyrimidine derivatives have been prepared and their inhibition activities against SARS-CoV 3CL protease were evaluated.

Structure–activity relationship (SAR) investigations of tetrahydroquinolines as BKCa agonists

pp 3573–3578

Vijay K. Gore*, Vu V. Ma, Ruoyuan Yin, Joe Ligutti, David Immke, Elizabeth M. Doherty, Mark H. Norman

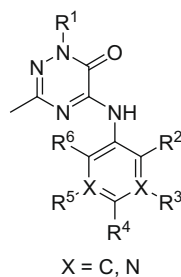


The synthesis and SAR of a series of novel class of potent tetrahydroquinoline BKCa agonists are reported.

5-Arylamino-1,2,4-triazin-6(1H)-one CRF₁ receptor antagonists

pp 3579–3583

William D. Schmitz*, Allison B. Brenner, Joanne J. Bronson, Jonathan L. Ditta, Corrine R. Griffin, Yu-Wen Li, Nicholas J. Lodge, Thaddeus F. Molski, Richard E. Olson, Xiaoliang Zhuo, John E. Macor

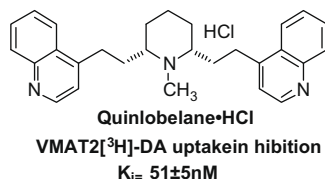


The structure–activity relationships of a series of 5-arylamino-1,2,4-triazin-6(1H)-ones as corticotropin releasing factor-1 receptor antagonists was investigated.

Quinlobelane: A water-soluble lobelane analogue and inhibitor of VMAT2

pp 3584–3587

Ashish P. Vartak, A. Gabriela Deaciuc, Linda P. Dwoskin, Peter A. Crooks*



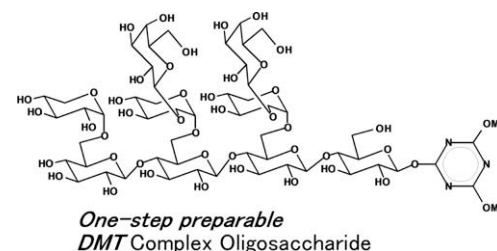
Replacing the phenyl rings of the VMAT2 inhibitor, lobelane with pyridyl, quinolyl and indolyl rings affords analogues with improved water solubility. The synthetic studies reported herein underscore the paucity of hydrogenation methods that offer selectivity between different classes of heteroaromatic lobelane analogues. Quinolyl rings were found to be the only replacement for the phenyl rings in lobelane that resulted in retention of VMAT2-inhibitory properties.

4,6-Dimethoxy-1,3,5-triazine oligoxyloglucans: Novel one-step preparable substrates for studying action of endo- β -1,4-glucanase III from *Trichoderma reesei*

pp 3588–3591

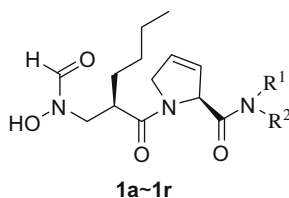
Atsushi Kobayashi, Tomonari Tanaka, Kazuhito Watanabe, Masaki Ishihara, Masato Noguchi, Hirofumi Okada, Yasushi Morikawa, Shin-ichiro Shoda*

Two kinds of 4,6-dimethoxy-1,3,5-triazine (DMT) oligoxyloglucans have been synthesized via one-step procedure starting from the corresponding unprotected oligoxyloglucans in water to study action of endo- β -1,4-*D*-glucanase III from *Trichoderma reesei*.

**Design, synthesis, and antibacterial activity of 2,5-dihydropyrrole formyl hydroxyamino derivatives as novel peptide deformylase inhibitors**

pp 3592–3595

Wei Shi, Yuejiao Duan, Yu Qian, Ming Li, Liping Yang, Wenhao Hu*

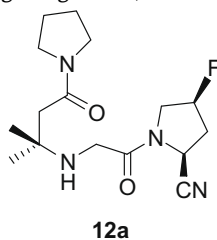


Design and synthesis of 2,5-dihydropyrrole formyl hydroxyamino derivatives as novel peptide deformylase inhibitors and their antibacterial activities against susceptible and resistant Gram-positive bacterial strains have been reported.

(2*S*,4*S*)-1-[2-(1,1-Dimethyl-3-oxo-3-pyrrolidin-1-yl-propylamino)acetyl]-4-fluoro-pyrrolidine-2-carbonitrile: A potent, selective, and orally bioavailable dipeptide-derived inhibitor of dipeptidyl peptidase IV

pp 3596–3600

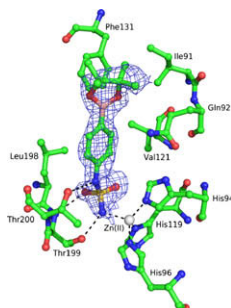
Teng-Kuang Yeh, Ting-Yueh Tsai, Tsu Hsu, Jai-Hong Cheng, Xin Chen, Jen-Shin Song, Horng-Shing Shy, Mei-Chun Chiou, Chia-Hui Chien, Ya-Ju Tseng, Chung-Yu Huang, Kai-Chia Yeh, Yu-Lin Huang, Chih-Hsiang Huang, Yu-Wen Huang, Min-Hsien Wang, Hung-Kuan Tang, Yu-Sheng Chao, Chiung-Tong Chen*, Weir-Torn Jiaang*

DPP-IV $IC_{50} = 15 \text{ nM}$

Carbonic anhydrase inhibitors: Crystallographic and solution binding studies for the interaction of a boron-containing aromatic sulfamide with mammalian isoforms I–XV

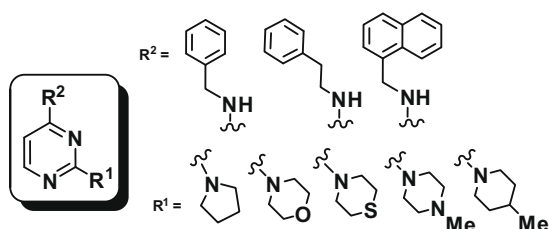
pp 3601–3605

Anna Di Fiore, Simona Maria Monti, Alessio Innocenti, Jean-Yves Winum, Giuseppina De Simone*, Claudiu T. Supuran*

**Design, synthesis and evaluation of 2,4-disubstituted pyrimidines as cholinesterase inhibitors**

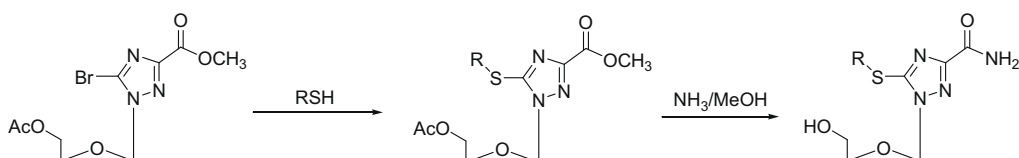
pp 3606–3609

Tarek Mohamed, Praveen P. N. Rao*

**S-Aryltriazole acyclonucleosides: Synthesis and biological evaluation against hepatitis C virus**

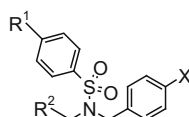
pp 3610–3613

Yang Liu, Yi Xia, Wei Li, Mei Cong, Alain Maggiani, Pieter Leyssen, Fanqi Qu, Johan Neyts, Ling Peng*

**Discovery of a novel series of CXCR3 antagonists**

pp 3614–3617

Stefano Crosignani*, Marc Missotten, Christophe Cleva, Ruggero Dondi, Yann Ratinaud, Yves Humbert, Ashis Baran Mandal, Agnès Bombrun, Christine Power, André Chollet, Amanda Proudfoot



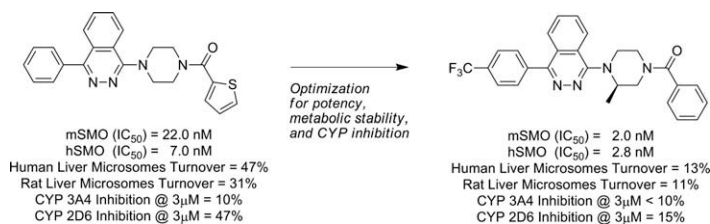
The discovery of a novel series of CXCR3 antagonists is described. Starting from an HTS positive, iterative optimization gave potent compounds (IC_{50} 15 nM in a chemotaxis assay). The strategy employed to improve the metabolic stability of these derivatives is described.



Design of 1-piperazinyl-4-arylphthalazines as potent Smoothed antagonists

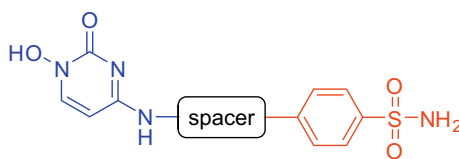
pp 3618–3622

Brian S. Lucas*, Wade Aaron, Songzhu An, Richard J. Austin, Matthew Brown, Hon Chan, Angela Chong, Randall Hungate, Tom Huang, Ben Jiang, Michael G. Johnson, Jacob A. Kaizerman, Gary Lee, Dustin L. McMinn, Jessica Orf, Jay P. Powers, Mingqing Rong, Maria M. Toteva, Craig Uyeda, Dineli Wickramasinghe, Guifen Xu, Qiuping Ye, Wendy Zhong

**New hydroxypyrimidinone-containing sulfonamides as carbonic anhydrase inhibitors also acting as MMP inhibitors**

pp 3623–3627

M. Alexandra Esteves, Osvaldo Ortet, Anabela Capelo, Claudiu T. Supuran, Sérgio M. Marques, M. Amélia Santos*

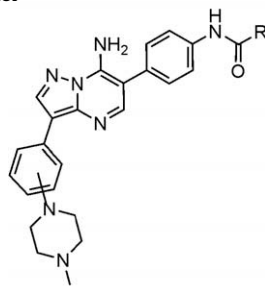


1: K_i (CAII) = 31 nM
 K_i (CAIX) = 3.4 nM

**New pyrazolo[1,5a]pyrimidines as orally active inhibitors of Lck**

pp 3628–3631

Nina Gommermann*, Peter Buehlmayer, Anette von Matt, Werner Breitenstein, Keiichi Masuya, Bernard Pirard, Pascal Furet, Sandra W. Cowan-Jacob, Gisbert Weckbecker

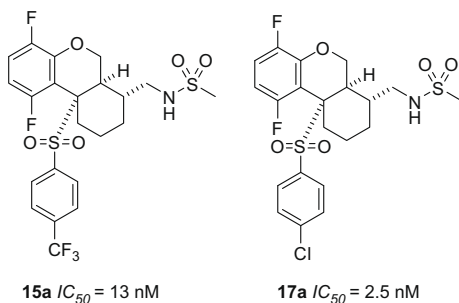


The preparation of pyrazolo[1,5a]pyrimidines and their evaluation as inhibitors of lymphocyte-specific kinase (Lck) both in vitro and in vivo is described.

Tricyclic sulfones as orally active γ -secretase inhibitors: Synthesis and structure–activity relationship studies

pp 3632–3635

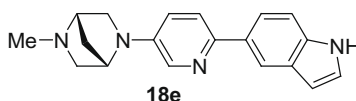
T. K. Sasikumar*, Li Qiang, Duane A. Burnett, David Cole, Ruo Xu, Hongmei Li, William J. Greenlee, John Clader, Lili Zhang, Lynn Hyde



Syntheses and structure–activity relationship (SAR) studies of 2,5-diazabicyclo[2.2.1]heptanes as novel $\alpha 7$ neuronal nicotinic receptor (NNR) ligands

pp 3636–3639

Tao Li*, William H. Bunnelle, Keith B. Ryther, David J. Anderson, John Malysz, Rosalind Helfrich, Jens H. Grønlien, Monika Håkerud, Dan Peters, Michael R. Schrimpf, Murali Gopalakrishnan, Jianguo Ji



A series of biaryl substituted 2,5-diazabicyclo[2.2.1]heptanes were synthesized as potent and selective $\alpha 7$ NNR agonists. Among them, compound **18e** shows a $\alpha 7$ binding affinity of 0.2 nM.

Synthesis and molecular modeling studies of 3-chloro-4-substituted-1-(8-hydroxy-quinolin-5-yl)-azetidin-2-ones as novel anti-filarial agents

pp 3640–3644

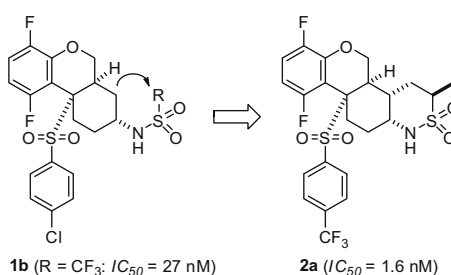
Santosh S. Chhajed*, Puranik Manisha, Virupaksha A. Bastikar, Halder Animeshchandra, V. N. Ingle, Chandrashekhar D. Upasani, Sachin S. Wazalwar

In the present investigation novel series of 4-substituted-1-(8-hydroxy-quinolin-5-yl)-azetidin-2-ones are synthesized, screened for in vitro anti-filarial activity against *Brugia malayi*. In silico molecular docking analysis of title compounds performed in to the active site of enzyme glutathione-S-transferases.

**Tetracyclic sulfones as potent γ -secretase inhibitors: Synthesis and structure–activity relationship studies**

pp 3645–3648

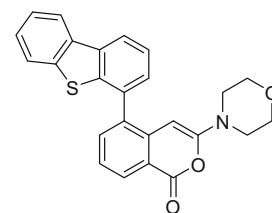
T. K. Sasikumar*, Duane A. Burnett, Theodros Asberom, Wen-Lian Wu, Chad Bennett, David Cole, Ruoxu Xu, William J. Greenlee, John Clader, Lili Zhang, Lynn Hyde

**Mapping the ATP-binding domain of DNA-dependent protein kinase (DNA-PK) with coumarin- and isocoumarin-derived inhibitors**

pp 3649–3653

Sara L. Payne, Sonsoles Rodriguez-Aristegui, Julia Bardos, Céline Cano, Bernard T. Golding, Ian R. Hardcastle, Marcus Peacock, Nahida Parveen, Roger J. Griffin*

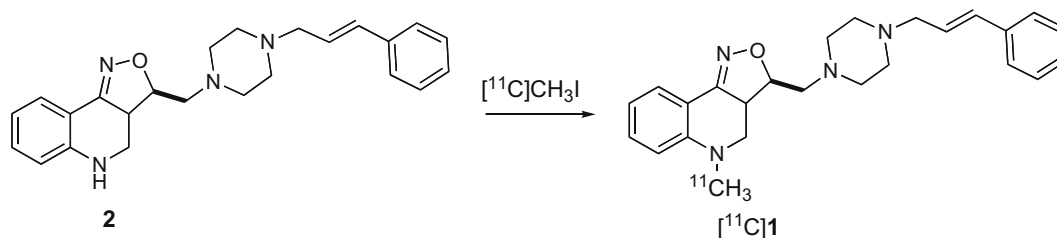
Replacement of the core heterocycle of a defined series of chromen-4-one DNA-PK inhibitors by the isomeric chromen-2-one (coumarin) and isochromen-1-one (isocoumarin) scaffolds was investigated. Structure-activity relationships for DNA-PK inhibition were broadly consistent, albeit with a reduction of potency compared with the parent chromenone.



Synthesis and in vivo evaluation of [^{11}C]MPTQ: A potential PET tracer for $\alpha 2\text{A}$ -adrenergic receptors

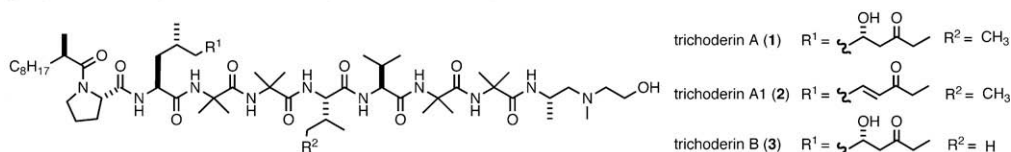
pp 3654–3657

Jaya Prabhakaran, Vattoly J. Majo, Matthew S. Milak, Pratap Mali, Lyudmila Savenkova, J. John Mann, Ramin V. Parsey, J. S. Dileep Kumar*

**Trichoderins, novel aminolipopeptides from a marine sponge-derived *Trichoderma* sp., are active against dormant mycobacteria**

pp 3658–3663

Patamaporn Pruksakorn, Masayoshi Arai, Naoyuki Kotoku, Catherine Vilch  ze, Anthony D. Baughn, Prashini Moodley, William R. Jacobs Jr., Motomasa Kobayashi*

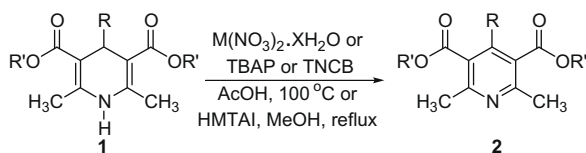


Three new aminolipopeptides, designated trichoderins A (1), A1 (2), and B (3), were isolated from a culture of marine sponge-derived fungus of *Trichoderma* sp. as anti-dormant mycobacterial substances.

Facile and efficient aromatization of 1,4-dihydropyridines with $\text{M}(\text{NO}_3)_2 \cdot x\text{H}_2\text{O}$, TNCB, TBAP and HMTAI and preparation of deuterium labeled dehydronifedipine from nifedipine- d_3

pp 3664–3668

Ajam C. Shaikh, Chinpiao Chen*



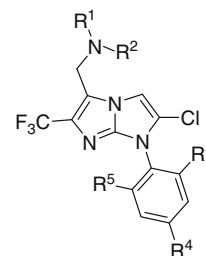
Facile aromatization of various 1,4-dihydropyridines was investigated using metal nitrates, TBAP, TNCB and HMTAI as oxidants. Efficient conversion of nifedipine- d_3 to dehydronifedipine- d_3 as an internal standard.

**Discovery of 6-chloro-2-trifluoromethyl-7-aryl-7H-imidazo[1,2-a]imidazol-3-ylmethylamines, a novel class of corticotropin-releasing factor receptor type 1 (CRF $_1$ R) antagonists**

pp 3669–3674

Dmitry Zuev*, Vivekananda M. Vrudhula, Jodi A. Michne, Bireswar Dasgupta, Sokhom S. Pin, Xiaohua Stella Huang, Dedong Wu, Qi Gao, Jie Zhang, Matthew T. Taber, John E. Macor, Gene M. Dubowchik*

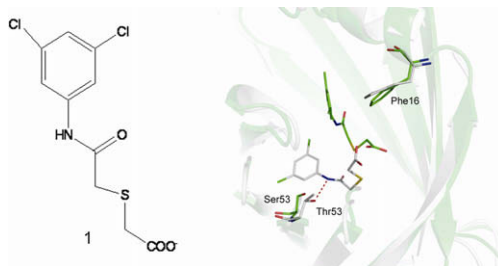
A novel series of [6-chloro-2-trifluoromethyl-7-aryl-7H-imidazo[1,2-a]imidazol-3-ylmethyl]-dialkylamines was discovered as potent CRF $_1$ R antagonists. The optimization of binding affinity in the series by the parallel reaction approach is discussed herein.



Discovery of highly selective inhibitors of human fatty acid binding protein 4 (FABP4) by virtual screening

pp 3675–3679

Haiyan Cai, Guirui Yan, Xiaodong Zhang, Olena Gorbenko, Heyao Wang*, Weiliang Zhu*

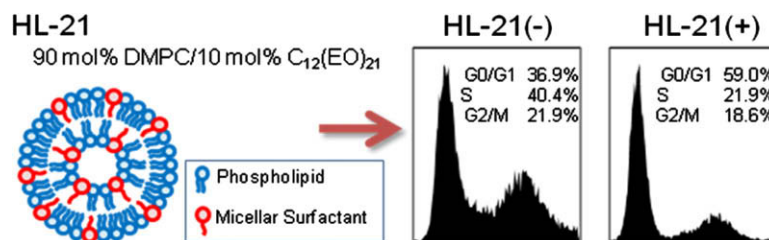


Compound **1** was identified as an inhibitor of human FABP4 with an IC_{50} of 13.5 μ M and it showed a selectivity more than 144-fold over human FABP3.

**Hybrid liposomes inhibit the growth of Cholangiocarcinoma by induction of cell cycle arrest in G₁ phase**

pp 3680–3682

Tomomi Towata, Yuji Komizu, Ryusho Kariya, Shinya Suzu, Yoko Matsumoto, Naoya Kobayashi, Chaisiri Wongkham, Sopit Wongkham, Ryuichi Ueoka*, Seiji Okada*

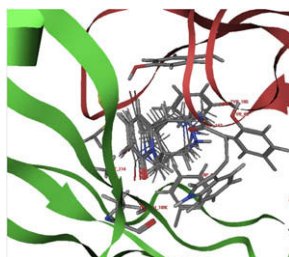


Hybrid liposomes composed of 90 mol % L- α -dimyristoylphosphatidylcholine (DMPC) and 10 mol % polyoxyethylene(21)dodecyl ether ($C_{12}(EO)_{21}$) specifically accumulated and induced cell cycle arrest in human cholangiocarcinoma cells.

In silico characterization of cytisinoids docked into an acetylcholine binding protein

pp 3683–3687

Juan Andrés Abin-Carriquiry*, Margot Paulino Zunini, Bruce K. Cassels, Susan Wonnacott, Federico Dajas

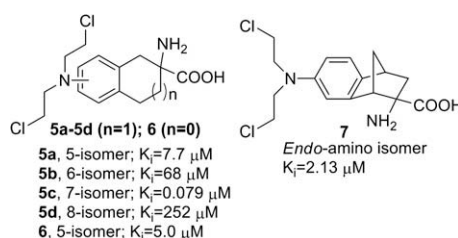


Cytisine and several derivatives docked into an acetylcholine binding protein of *Lymnaea stagnalis* (Ls-AChBP), taken as a model of the agonist binding site of neuronal nicotinic acetylcholine receptor (nAChR). A strong correlation was found between the docking energies and experimental pIC_{50} values.

Regiospecific and conformationally restrained analogs of melphalan and DL-2-NAM-7 and their affinities for the large neutral amino acid transporter (system LAT1) of the blood–brain barrier

pp 3688–3691

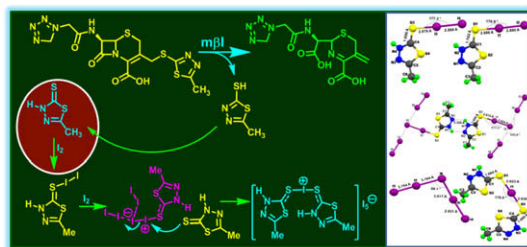
Jyothi Matharu, Jun Oki, David R. Worthen, Quentin R. Smith, Peter A. Crooks*



Placing the mustard moiety at C-7 of the tetralin ring (**5c**) affords greatest affinity for the System LAT1 transporter; the more conformationally restrained analogs (**6** and **7**) of DL-2-NAM-7 had lower affinity than **5c**.

Interaction of heterocyclic thiols/thiones eliminated from cephalosporins with iodine and its biological implications pp 3692–3697

A. Tamilselvi, Govindasamy Mugesh*

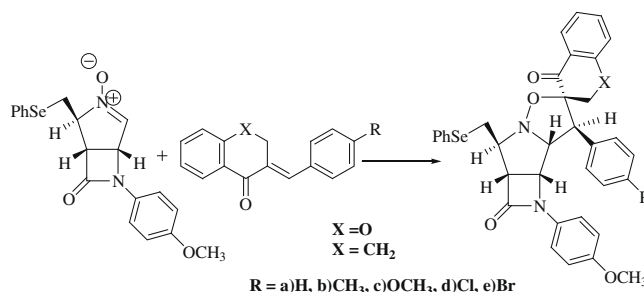


This study provides the first experimental evidence that the heterocyclic side chains present in cephalosporins not only inhibits peroxidase-catalyzed iodination reactions, but also reacts with iodine to produce stable charge-transfer complexes. The peroxidase inhibition and reactivity toward iodine must be taken into account while designing new antibiotics based on cephalosporins as these activities may adversely affect the thyroid activity.



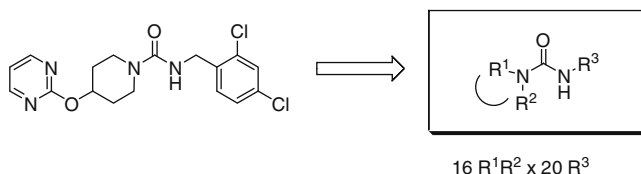
Synthesis of novel β -lactam fused spiroisoxazolidine chromanones and tetralones as potent antimicrobial agent for human and plant pathogens pp 3698–3702

Natarajan Arumugam, Raghavachary Raghunathan*, Vellaisamy Shanmugaiah, Narayanasamy Mathivanan



Rapid synthesis of an array of trisubstituted urea-based soluble epoxide hydrolase inhibitors facilitated by a novel solid-phase method pp 3703–3707

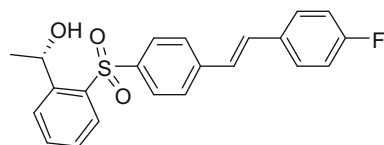
Jennifer A. Kowalski*, Alan D. Swinamer, Ingo Muegge, Anne B. Eldrup, Alison Kukulka, Charles L. Cywin, Stéphane De Lombaert



Rapid exploration of multi-dimensional SAR around a series of trisubstituted urea inhibitors of sEH was accomplished using a focused library approach.

Non-basic ligands for aminergic GPCRs: The discovery and development diaryl sulfones as selective, orally bioavailable 5-HT_{2A} receptor antagonists for the treatment of sleep disorders pp 3708–3712

Tammy Ladduwahetty*, Myra Gilligan, Alexander Humphries, Kevin J. Merchant, Rebecca Fish, George McAlister, Magnus Ivarsson, Maria Dominguez, Desmond O'Connor, Angus M. MacLeod



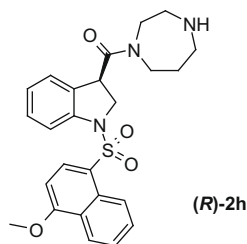
11 h5HT_{2A} 0.22nM
% occupancy (1mg/kg p.o.) 83%

Herein is described the development of a non-basic series of aryl sulfones as 5-HT_{2A} receptor antagonists with excellent receptor occupancy on oral dosing *in vivo*.

The discovery and SAR of indoline-3-carboxamides—A new series of 5-HT₆ antagonists

pp 3713–3716

Mark Reid*, Ian Carlyle, Wilson L. Caulfield, Tom R. Clarkson, Fiona Cusick, Ola Epemolu, Robert Gilfillan, Richard Goodwin, David Jaap, Elise C. O'Donnell, Jeremy Presland, Zoran Rankovic*, Daniel Spinks, Gayle Spinks, Anne M. Thomson, Fiona Thomson, James Strain, Grant Wishart

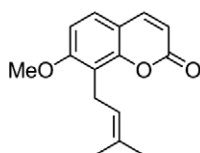


We report the identification and SAR around *N*-(2-aminoalkyl)-1-(arylsulfonyl)indoline-3-carboxamides—a novel chemotype of 5-HT₆ antagonists.

Prenylcoumarin with Rev-export inhibitory activity from *Cnidii Monnieri* Fructus

pp 3717–3720

Satoru Tamura, Toshiaki Fujitani, Masafumi Kaneko, Nobutoshi Murakami*



osthol (1)
IC₅₀=1.6 μM

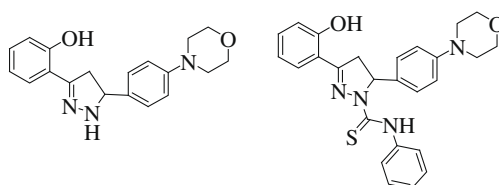
Inhibitor for Rev-export
from the crude drug
Cnidii Monnieri Fructus

Prenylcoumarin osthol (1) was disclosed as the new Rev-export inhibitor from *Cnidii Monnieri* Fructus. Both prenyl residue and carbonyl conjugated double bond were revealed to play an important role in the biological potency of 1.

Synthesis, analgesic and anti-inflammatory activities of some novel pyrazolines derivatives

pp 3721–3725

Ratnadeep S. Joshi, Priyanka G. Mandhane, Santosh D. Diwakar, Sanjay K. Dabhade, Charansingh H. Gill*

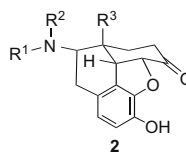


In search for a new analgesic and anti-inflammatory agent with improved potency, we designed and synthesized a series of 3,2-(4,5-dihydro-5-(4-morpholinophenyl)-1H-pyrazol-3-yl)phenols **6(a–g)** and its *N*-phenylpyrazol-1-carbothioamide **7(a–g)** by Claisan–Schmidt condensation followed by the reaction of hydrazine hydrate. All the synthesized compounds were assayed for their *in vivo* analgesic and anti-inflammatory activities. All the compounds synthesized showed the potential to demonstrate analgesic and anti-inflammatory activity, of particular interest compounds **6a**, **6b**, **6g**, **7a**, **7d** and **7g** were found comparable to Diclofenac.

Investigation of Beckett–Casy model 2: Synthesis of novel 15–16 nornaltrexone derivatives and their pharmacology

pp 3726–3729

Hiroshi Nagase*, Satomi Imaide, Miyuki Tomatsu, Toru Nemoto, Mayumi Nakajima, Kaoru Nakao, Hidenori Mochizuki, Hideaki Fujii

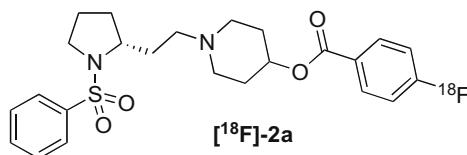


Novel 15–16 nornaltrexone derivatives **2** were synthesized using a double decarboxylation reaction as the key reaction to examine the Beckett–Casy model.

Looking for a 5-HT₇ radiotracer for positron emission tomography

pp 3730–3733

Julien Andriès, Laëtitia Lemoine, Alice Mouchel-Blaisot, Sandrine Tang, Mathieu Verdurand, Didier Le Bars, Luc Zimmer, Thierry Billard*

**Structure-based prediction and biosynthesis of the major mammalian metabolite of the cardioactive prototype LASSBio-294**

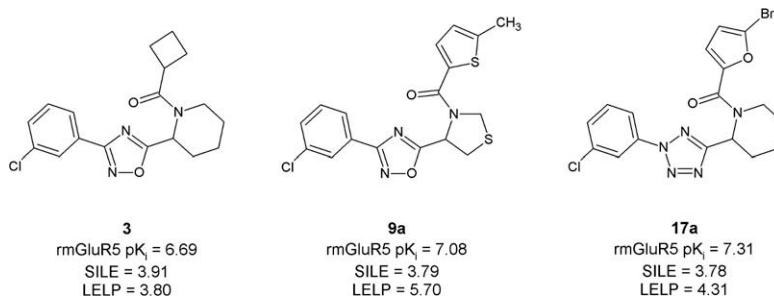
pp 3734–3736

Emmanuel O. Carneiro, Carolina H. Andrade, Rodolpho C. Braga, Andréa C. B. Tôrres, Rosângela O. Alves, Luciano M. Lião, Carlos A. M. Fraga, Eliezer J. Barreiro, Valéria de Oliveira*

**Hit-to-lead optimization of disubstituted oxadiazoles and tetrazoles as mGluR5 NAMs**

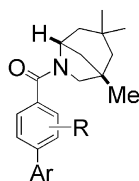
pp 3737–3741

Gábor Wágner*, Csaba Wéber, Olga Nyéki, Katalin Nógrádi, Attila Bielik, László Molnár, Amrita Bobok, Attila Horváth, Béla Kiss, Sándor Kolok, József Nagy, Dalma Kurkó, Krisztina Gál, István Greiner, Zolt Szombathelyi, György M. Keserű, György Domány

**Synthesis and evaluation of azabicyclo[3.2.1]octane derivatives as potent mixed vasopressin antagonists**

pp 3742–3745

Aimee L. Crombie*, Thomas M. Antrilli, Brandon A. Campbell, David L. Crandall, Amedeo A. Failli, Yanan He, Jeffrey C. Kern, William J. Moore, Lisa M. Nogle, Eugene J. Trybulski

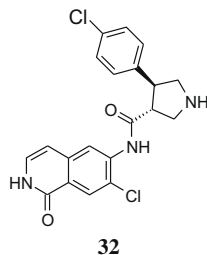


A series of biaryl amides containing an azabicyclo[3.2.1]octane amine headpiece were synthesized and evaluated as mixed arginine vasopressin (AVP) receptor antagonists.

Substituted 2H-isoquinolin-1-ones as potent Rho-kinase inhibitors: Part 3, aryl substituted pyrrolidines

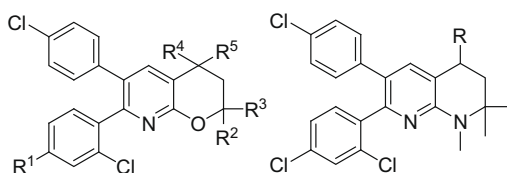
pp 3746–3749

Todd Bosanac*, Eugene R. Hickey, John Ginn, Mohammed Kashem, Steven Kerr, Stanley Kugler, Xiang Li, Alan Olague, Sabine Schlyer, Erick R. R. Young

**Dihydro-pyrano[2,3-b]pyridines and tetrahydro-1,8-naphthyridines as CB1 receptor inverse agonists: Synthesis, SAR and biological evaluation**

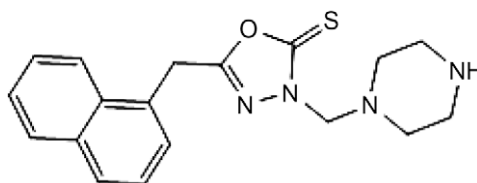
pp 3750–3754

Christina B. Madsen-Duggan*, John S. Debenham*, Thomas F. Walsh, Lin Yan, Pei Huo, Junying Wang, Xinchun Tong, Julie Lao, Tung M. Fong, Jing Chen Xiao, Cathy R.-R. C. Huang, Chun-Pyn Shen, D. Sloan Stribling, Lauren P. Shearman, Alison M. Strack, Mark T. Goulet, Jeffrey J. Hale

**Synthesis and biological activity of oxadiazole and triazolothiadiazole derivatives as tyrosinase inhibitors**

pp 3755–3759

Kok Wai Lam, Ahmad Syahida, Zaheer Ul-Haq, Mohd. Basyaruddin Abdul Rahman, Nordin H. Lajis*

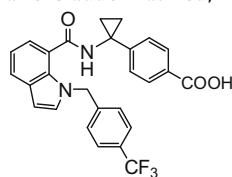


A series of oxadiazole and triazolothiadiazole derivatives were synthesized and evaluated their mushroom tyrosinase inhibitory activities. Compound 5 exhibited highest tyrosinase inhibitory activity with IC₅₀ value of 0.87 ± 0.16 μM.

**Discovery of 4-{1-[(1-[4-(trifluoromethyl)benzyl]-1H-indol-7-yl)carbonyl]amino}cyclopropyl}benzoic acid (MF-766), a highly potent and selective EP₄ antagonist for treating inflammatory pain**

pp 3760–3763

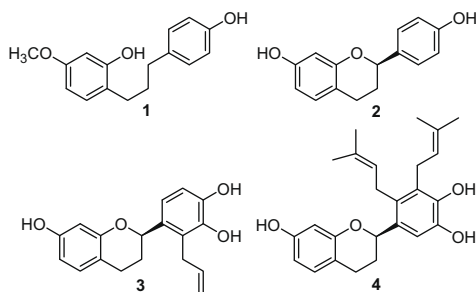
John Colucci, Michael Boyd, Carl Berthelette, Jean-Francois Chiasson, Zhaoyin Wang, Yves Ducharme, Rick Friesen, Mark Wrona, Jean-Francois Levesque, Danielle Denis, Marie-Claude Mathieu, Rino Stocco, Alex G. Therien, Patsy Clarke, Steve Rowland, Daigen Xu, Yongxin Han*

**MF-766**EP₄ K_i = 0.23 nMEP₄ functional IC₅₀ = 1.3 nMIn vivo AIA ED₁₀₀ = 0.025 mg/kg/day

New estrogenic compounds isolated from *Broussonetia kazinoki*

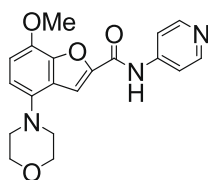
pp 3764–3767

Da Yeon Lee, Do Hee Kim, Hwa Jin Lee, YoungJoo Lee, Kwang Hee Ryu, Bo-In Jung, Yun Seon Song, Jae-Ha Ryu*

Four estrogenic compounds, broussonin A (1), tupichinol C (2), kazinol U (3), and (+)-(2R) kazinol I (4) were identified from *Broussonetia kazinoki*.**Synthetic studies on selective adenosine A_{2A} receptor antagonists. Part II: Synthesis and structure–activity relationships of novel benzofuran derivatives**

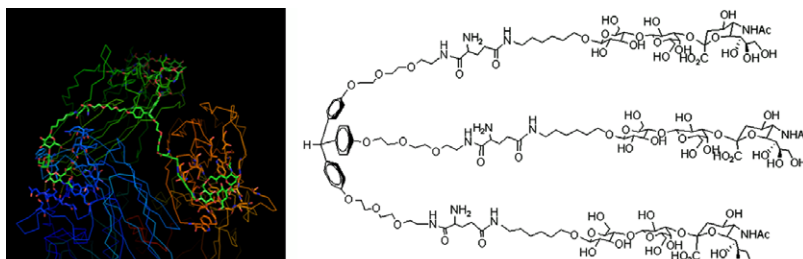
pp 3768–3771

Osamu Saku*, Mayumi Saki, Masako Kurokawa, Ken Ikeda, Shin-ichi Uchida, Takuya Takizawa, Noriaki Uesaka

The discovery of a novel series of A_{2A} antagonists is described. A selected compound was shown to be able to induce anti-parkinsonian effects in MPTP-treated common marmosets.**Novel trivalent anti-influenza reagent**

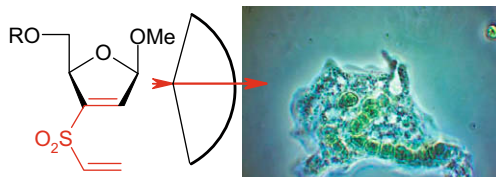
pp 3772–3776

Fei Feng, Nobuaki Miura, Norikazu Isoda, Yoshihiro Sakoda, Masatoshi Okamatsu, Hiroshi Kida*, Shin-Ichiro Nishimura*

A trivalent anti-influenza reagent with sialyllactose at the terminals shows ~85% inhibition against influenza virus infection in an assay with MDCK cells at the concentration of 400 μ M.**First synthesis and antiprotozoal activities of divinyl sulfone-modified carbohydrates**

pp 3777–3780

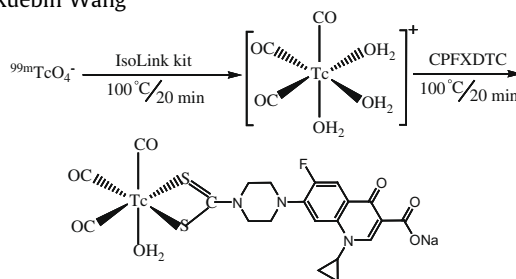
Tarun Kumar Pal, Tuli Dey, Arindam Chakrabarty, Debanjana Dey, Sudip K. Ghosh*, Tanmaya Pathak*

Divinyl sulfone-modified carbohydrates have been synthesized for the first time by reacting carbohydrate epoxides with thioethanol and one of the modified divinyl sulfones initiated significant cell death in *Entamoeba* species.

Synthesis and biological evaluation of a novel $^{99m}\text{Tc}(\text{CO})_3$ complex of ciprofloxacin dithiocarbamate as a potential agent to target infection

pp 3781–3784

Junbo Zhang*, Shijian Zhang, Haixun Guo, Xuebin Wang

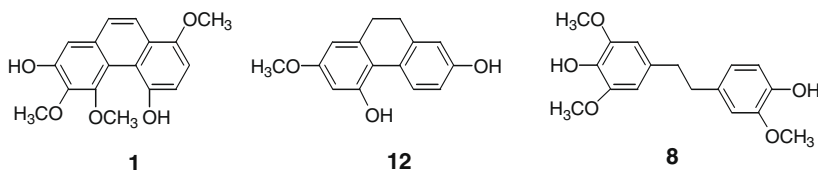


The ciprofloxacin dithiocarbamate (CPFXDTC) was radiolabeled with $^{99m}\text{Tc}(\text{CO})_3(\text{H}_2\text{O})_3]^+$ intermediate to form the $^{99m}\text{Tc}(\text{CO})_3$ -CPFXDTC complex in high yield. The biodistribution and SPECT imaging studies reveal its good biological features as an infection imaging agent.

Phenanthrenes from *Dendrobium nobile* and their inhibition of the LPS-induced production of nitric oxide in macrophage RAW 264.7 cells

pp 3785–3787

Ji Sang Hwang, Seon A Lee, Seong Su Hong, Xiang Hua Han, Chul Lee, Shin Jung Kang, Dongho Lee, Youngsoo Kim, Jin Tae Hong, Mi Kyeong Lee, Bang Yeon Hwang*



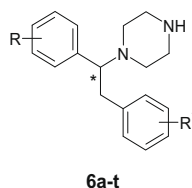
A new phenanthrene, 3,4,8-trimethoxyphenanthrene-2,5-diol (**1**), along with nine known phenanthrenes and three known bibenzyls was isolated from *Dendrobium nobile*. All of the isolates were evaluated for their potential to inhibit the LPS-induced NO production in murine macrophage RAW 264.7 cells.

Second generation *N*-(1,2-diphenylethyl)piperazines as dual serotonin and noradrenaline reuptake inhibitors: Improving metabolic stability and reducing ion channel activity

pp 3788–3792

M. Jonathan Fray, Paul V. Fish*, Gillian A. Allan, Gerwyn Bish, Nick Clarke, Rachel Eccles, Anthony C. Harrison, Jean-Loic Le Net, Stephen C. Phillips, Nicola Regan, Cecile Sobry, Alan Stobie, Florian Wakenhut, Dominique Westbrook, Simon L. Westbrook, Gavin A. Whitlock

New *N*-(1,2-diphenylethyl)piperazines **6** are disclosed as dual serotonin and noradrenaline reuptake inhibitors (SNRI). Piperazine (–)-**6a** was identified as a potent and selective dual SNRI with improved metabolic stability and reduced ion channel activity when compared to previous examples.

e.g. (–)-**6a**: R = H; R' = 2-OMe

SRI, $K_i = 2$ nM
NRI, $K_i = 12$ nM
DRI, $K_i = 2940$ nM

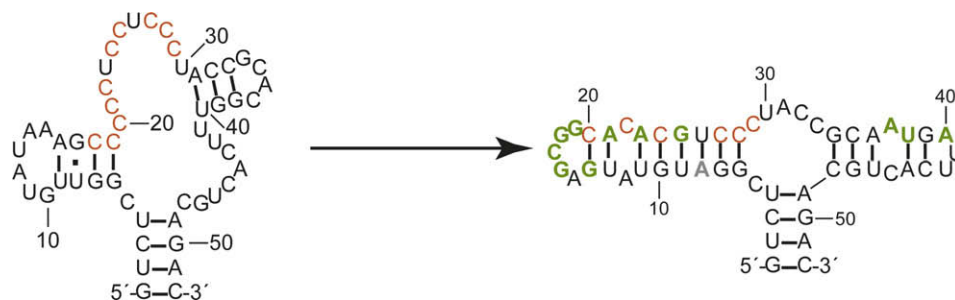
HLM, $T_{1/2} > 120$ min
CYP2D6-i, $\text{IC}_{50} = >30,000$ nM
 K^+ hERG, $\text{IC}_{50} = 22,900$ nM
 Na^+ TTX-S, $\text{IC}_{50} = 5400$ nM

R = H; 2-F; 3-F; 4-F * = RS, R or S
R' = OMe; OnPr; OiPr; OcPr; OCH_2cPr ; OCHF_2 ; OCF_3 ; 2,3- OCH_2CH_2 -

Evolution of specific RNA motifs derived from pan-protein interacting precursors

pp 3793–3796

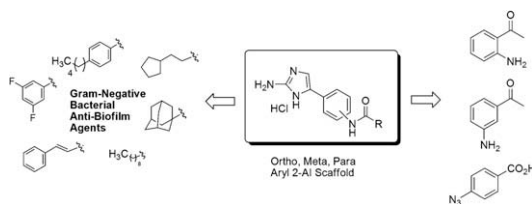
Marie-Sophie L. Ahmed, Günter Mayer*



Identification of aryl 2-aminoimidazoles as biofilm inhibitors in Gram-negative bacteria

pp 3797–3800

Cynthia A. Bunders, Justin J. Richards, Christian Melander*



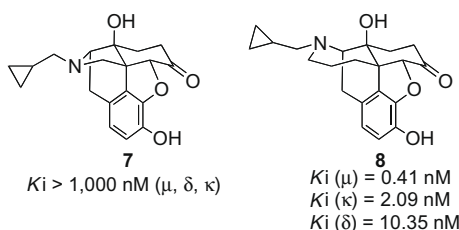
The synthesis and biofilm inhibitory activity of a 30-member aryl amide 2-aminoimidazole library against the three biofilm forming Gram-negative bacteria *Escherichia coli*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* is presented. The most active compound identified inhibits the formation of *E. coli* biofilms with an IC_{50} of 5.2 μ M and was observed to be non-toxic to planktonic growth, demonstrating that analogues based on an aryl framework are viable options as biofilm inhibitors within the 2-aminoimidazole family.



Investigation of Beckett–Casy model 3: Synthesis of novel naltrexone derivatives with contracted and expanded D-rings and their pharmacology

pp 3801–3804

Hiroshi Nagase*, Satomi Imaide, Miyuki Tomatsu, Shigeto Hirayama, Toru Nemoto, Noriko Sato, Mayumi Nakajima, Kaoru Nakao, Hidenori Mochizuki, Hiroaki Gouda, Shuichi Hirono, Hideaki Fujii

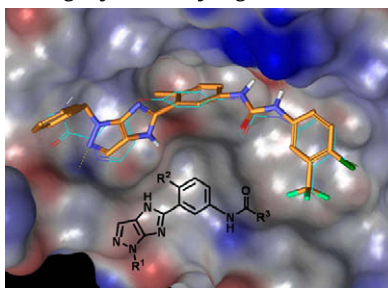


Novel naltrexone derivatives **7** and **8** were synthesized to examine the Beckett–Casy model.

1,4-Dihydropyrazolo[4,3-d]imidazole phenyl derivatives: A novel type II Raf kinase inhibitors

pp 3805–3808

Hana Yu, Yunkyung Jung, Hwan Kim, Junghun Lee, Chang-Hyun Oh, Kyung Ho Yoo, Taebo Sim, Jung-Mi Hah*

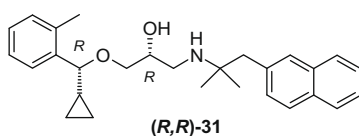


A series 1,4-dihydropyrazolo[4,3-d]imidazole phenyl derivatives and their antiproliferative activities against A375P human melanoma cell line and WM3629 cell line were described.

New aminopropandiol derivatives as orally available and short-acting calcium-sensing receptor antagonists

pp 3809–3813

Yuko Shinagawa*, Teruhiko Inoue, Kazuyuki Hirata, Takeo Katsushima*, Takashi Nakagawa, Yushi Matsuo, Masanori Shindo, Hiromasa Hashimoto*

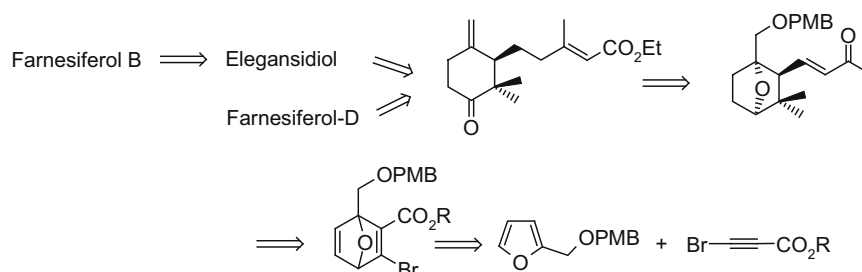


The discovery of an orally available and short-acting calcium-sensing receptor antagonist (*R,R*)-**31** is reported.

Total synthesis of (±)-elegansidiol, (±)-farnesiferol B, and (±)-farnesiferol D

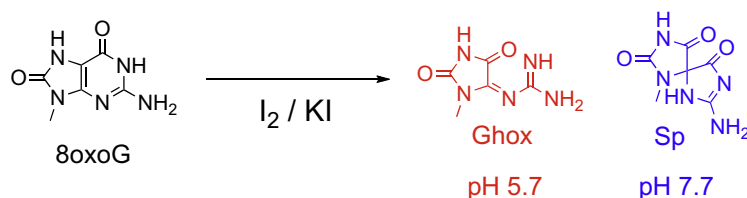
pp 3814–3817

Jhillu Singh Yadav*, Kamani Satyanarayana, Pamu Sreedhar, Pabbaraja Srihari, Thokhir Basha Shaik, Shasi Vardhan Kalivendi

**The oxidation of 8-oxo-7,8-dihydroguanine by iodine**

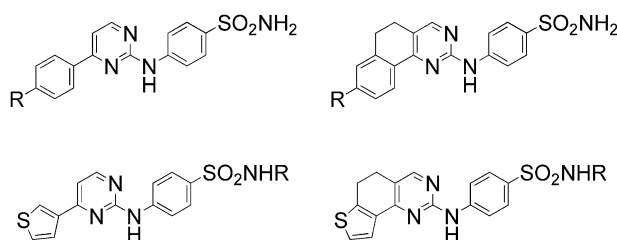
pp 3818–3820

Katsuhito Kino*, Masayuki Morikawa, Teruhiko Kobayashi, Takanobu Kobayashi, Rie Komori, Yoshihisa Sei, Hiroshi Miyazawa

**Synthesis and biological evaluation of tricyclic anilinopyrimidines as IKKβ inhibitors**

pp 3821–3825

Aimee L. Crombie*, Fuk-Wah Sum, Dennis W. Powell, Darrin W. Hopper, Nancy Torres, Dan M. Berger, Yixian Zhang, Maria Gavril, Tammy M. Sadler, Kim Arndt

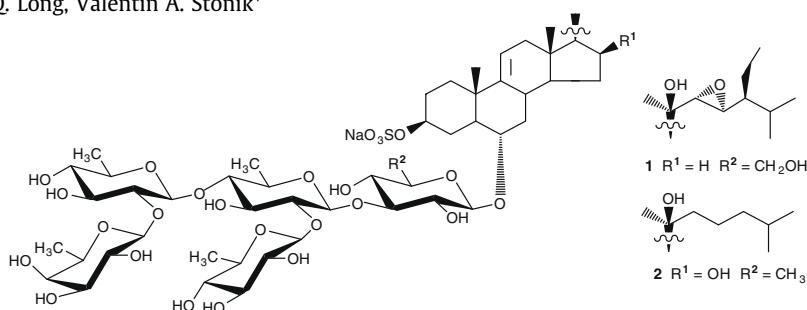


A series of anilinopyrimidines and their tricyclic analogues were synthesized and evaluated as IKKβ inhibitors.

Two new asterosaponins, archasterosides A and B, from the Vietnamese starfish *Archaster typicus* and their anticancer properties

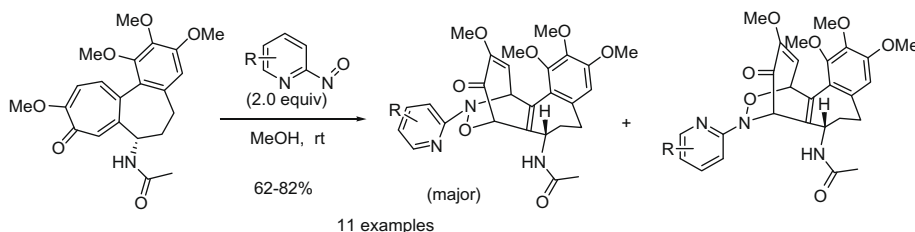
pp 3826–3830

Alla A. Kicha, Natalia V. Ivanchina, Trinh T. T. Huong, Anatoly I. Kalinovsky, Pavel S. Dmitrenok, Sergey N. Fedorov, Sergey A. Dyshlovoy, Pham Q. Long, Valentin A. Stonik*



Syntheses and biological evaluation of ring-C modified colchicine analogs**pp 3831–3833**

Baiyuan Yang, Zhiqing C. Zhu, Holly V. Goodson, Marvin J. Miller*

**OTHER CONTENT****Corrigendum****p 3834**

*Corresponding author

Supplementary data available via ScienceDirect

COVER

Overlay of high resolution co-crystal structures of *R*-**22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, 17, 5677.]

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