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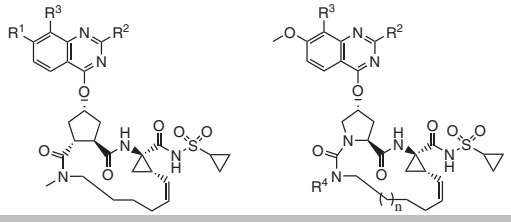
BMCL DIGEST

Synthesis and SAR of potent inhibitors of the Hepatitis C virus NS3/4A protease: Exploration of P2 quinazoline substituents pp 4004–4011

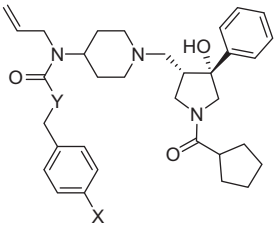
Magnus Nilsson, Anna Karin Belfrage, Stefan Lindström, Horst Wähling, Charlotta Lindquist, Susana Ayesa, Pia Kahnberg, Mikael Pelcman, Kurt Benkestock, Tatiana Agback, Lotta Vrang, Ylva Terelius, Kristina Wikström, Elizabeth Hamelink, Christina Rydergård, Michael Edlund, Anders Eneroth, Pierre Raboisson, Tse-I Lin, Herman de Kock, Piet Wigerinck, Kenneth Simmen, Bertil Samuelsson, Åsa Rosenquist*



REGULAR ARTICLES

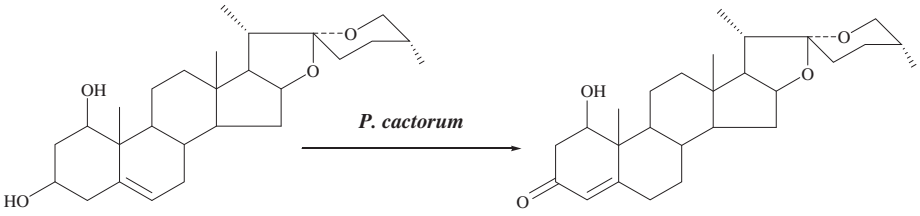
Studies on the structure–activity relationship of 1,3,3,4-tetra-substituted pyrrolidine embodied CCR5 receptor antagonists. Part 1: Tuning the N-substituents pp 4012–4014

Li Ben, Eric Dale Jones, Enkun Zhou, Chen Li, Dean Cameron Baylis, Shanghai Yu, Miao Wang, Xing He, Jonathan Alan Victor Coates, David Ian Rhodes, Gang Pei, John Joseph Deadman, Xin Xie*, Dawei Ma*



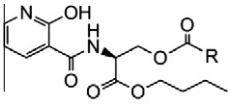
One unique steroidal sapogenin obtained through the microbial transformation of ruscogenin by *Phytophthora cactorum* ATCC 32134 and its potential inhibitory effect on tissue factor (TF) procoagulant activity pp 4015–4017

Nai-Dong Chen, Lei Yue, Jian Zhang*, Jun-Ping Kou, Bo-Yang Yu*



One unique steroidal sapogenin, 1-hydroxyspirost-4-en-3-one, which showed great inhibitory effect on tissue factor procogulant activity was obtained through the microbial transformation of ruscogenin by *Phytophthora cactorum* ATCC 32134. The stereochemical assignments of this metabolite were made unambiguously for the first time using 2D NMR spectroscopy.

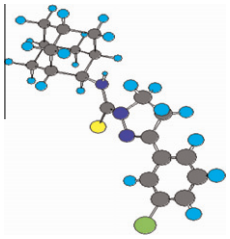
Synthesis and biological activity of 2-hydroxynicotinoyl-serine-butyl esters related to antibiotic UK-3A **pp 4018–4020**
Ade Arsianti*, Muhammad Hanafi, Endang Saepudin, Tsumoru Morimoto, Kiyomi Kakiuchi



AD-1, R = CH_3
AD-2, R = $C_6H_5C_2H_4$
AD-3, R = C_7H_{15}

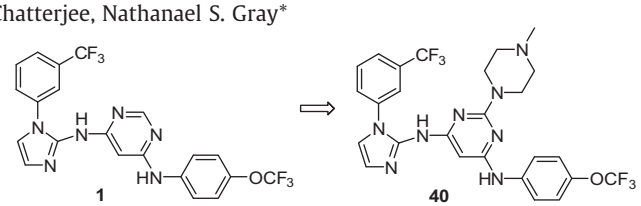
Three novel 2-hydroxynicotinoyl-serine-butyl esters, **AD-1**, **AD-2** and **AD-3** have been synthesized and subsequently evaluated on the basis of their toxicity levels and antibiotic activities. **AD-3** demonstrated significant activity as a growth inhibitor of *Bacillus subtilis* and *Staphylococcus aureus*.

Exploring structural requirements of 1-N-substituted thiocarbamoyl-3-phenyl-2-pyrazolines as antiamoebic agents using comparative QSAR modelling **pp 4021–4026**
Nilanjan Adhikari, Milan Kumar Maiti, Tarun Jha*



To find structural requirements for more active antiamoebic agents than metronidazole, comparative QSAR modelling was done on thirty 1-N-substituted thiocarbamoyl-3-phenyl-2-pyrazolines using PCRA, stepwise regression, FA-MLR and PLS techniques.

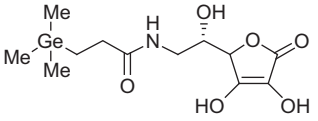
Discovery of novel 1*H*-imidazol-2-yl-pyrimidine-4,6-diamines as potential antimalarials **pp 4027–4031**
Xianming Deng, Advait Nagle, Tao Wu, Tomoyo Sakata, Kerstin Henson, Zhong Chen, Kelli Kuhen, David Plouffe, Elizabeth Winzeler, Francisco Adrian, Tove Tuntland, Jonathan Chang, Susan Simerson, Steven Howard, Jared Ek, John Isbell, David C. Tully, Arnab K. Chatterjee, Nathanael S. Gray*



1 3D7 EC_{50} = 436 nM
40 3D7 EC_{50} = 34 nM

A novel family of 1*H*-imidazol-2-yl-pyrimidine-4,6-diamines has been identified with potent activity against the erythrocyte-stage of *Plasmodium falciparum* (*Pf*), the most common causative agent of malaria. A systematic SAR study resulted in the identification of compound **40** which exhibits good potency against both wild-type and drug resistant parasites and exhibits good in vivo pharmacokinetic properties.

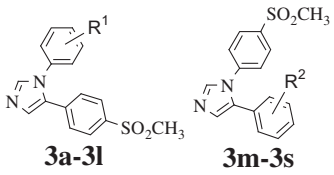
A novel organogermanium protected atopic dermatitis induced by oxazolone **pp 4032–4034**
Doo Hyeon Lim, Minghua Li, Jung-A Seo, Kyung-Min Lim, Seung Wook Ham*



A organogermanium derivative was synthesized and evaluated for anti-AD activities.

1,5-Diarylimidazoles with strong inhibitory activity against COX-2 catalyzed PGE_2 production from LPS-induced RAW 264.7 cells **pp 4035–4037**

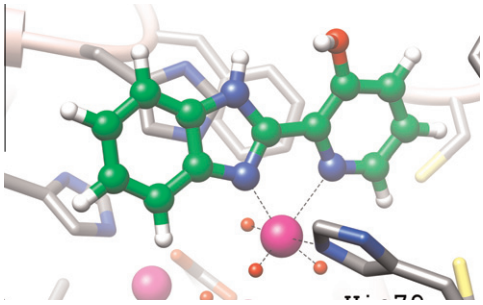
Haiyan Che, Truong Ngoc Tuyen, Hyun Pyo Kim, Haeil Park*



A series of 1,5-diarylimidazoles with 4-methylsulfonylphenyl group were prepared and evaluated for the inhibitory activities against COX-2 catalyzed PGE_2 production from LPS-induced RAW 264.7 cells. Most of synthesized 1,5-diarylimidazoles exhibited strong inhibitory activities regardless of the position of the 4-methylsulfonylphenyl group. The 1,5-diarylimidazoles with a halogen atom (**3c**–**3h**, **3n**–**3p**) gave mostly excellent inhibitory activities regardless of the position and species of the halogen atom. Whereas the 1,5-diarylimidazoles with two fluorine atoms (**3k**, **3l**, **3r**, **3s**) showed rather reduced inhibitory activities.

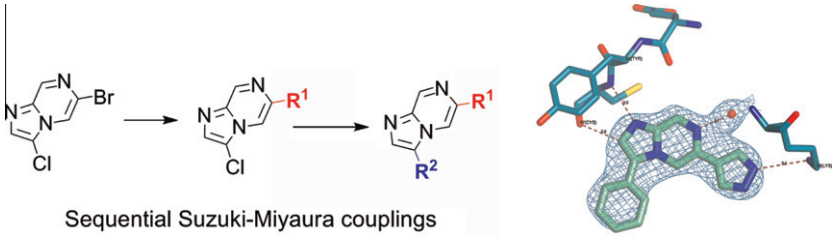
Subtype-selectivity of metal-dependent methionine aminopeptidase inhibitors **pp 4038–4044**

Markus A. Altmeyer, Aline Marschner, Rolf Schiffmann, Christian D. Klein*



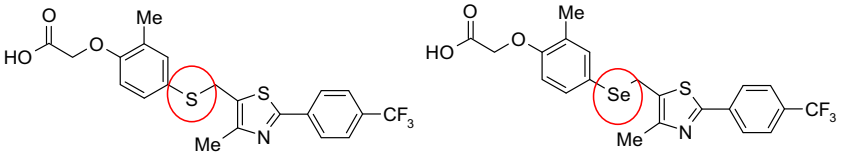
Design and evaluation of 3,6-di(hetero)aryl imidazo[1,2-*a*]pyrazines as inhibitors of checkpoint and other kinases **pp 4045–4049**

Thomas P. Matthews*, Tatiana McHardy, Suki Klair, Kathy Boxall, Martin Fisher, Michael Cherry, Charlotte E. Allen, Glynn J. Addison, John Ellard, G. Wynne Aherne, Isaac M. Westwood, Rob van Montfort, Michelle D. Garrett, John C. Reader, Ian Collins

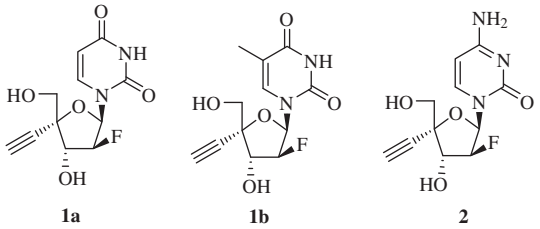


Synthesis of isosteric selenium analog of the PPARβ/δ agonist GW501516 and comparison of biological activity **pp 4050–4052**

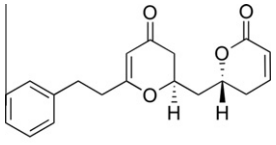
Arun K. Sharma*, Ugir Hossain Sk, Pengfei He, Jeffrey M. Peters, Shantu Amin



Synthesis and anti-HIV activity of 2′-deoxy-2′-fluoro-4′-C-ethynyl nucleoside analogs **pp 4053–4056**
Qiang Wang, Yanfeng Li, Chuanjun Song, Keduo Qian, Chin-Ho Chen, Kuo-Hsiung Lee*, Junbiao Chang*



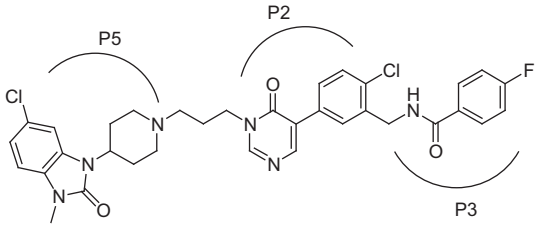
7′,8′-Dihydroobolactone, a typanocidal α-pyrone from the rainforest tree *Cryptocarya obovata* **pp 4057–4059**
Rohan A. Davis, Ozlem Demirkiran, Melissa L. Sykes, Vicky M. Avery, Lekha Suraweera, Gregory A. Fechner, Ronald J. Quinn*



7', 8'-Dihydroobolactone
IC_{50} = 2.8 μM (*T. b. brucei*)

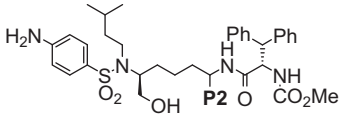
The isolation and structure elucidation of a new trypanocidal α-pyrone, 7′,8′-dihydroobolactone, is reported.

Diazinones as P2 replacements for pyrazole-based cathepsin S inhibitors **pp 4060–4064**
Michael K. Ameriks*, Scott D. Bembenek, Matthew T. Burdett, Ingrid C. Choong, James P. Edwards, Damara Gebauer, Yin Gu, Lars Karlsson, Hans E. Purkey, Bart L. Staker, Siquan Sun, Robin L. Thurmond, Jian Zhu



hCatS IC_{50} = 40 nM

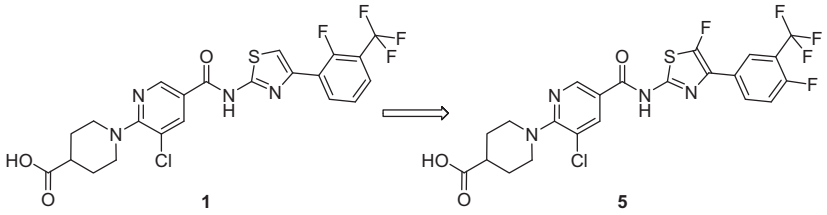
Epsilon substituted lysinol derivatives as HIV-1 protease inhibitors **pp 4065–4068**
Kristen L. G. Jones*, M. Katharine Holloway, Hua-Poo Su, Steven S. Carroll, Christine Burlein, Sinoeun Touch, Daniel J. DiStefano, Rosa I. Sanchez, Theresa M. Williams, Joseph P. Vacca, Craig A. Coburn



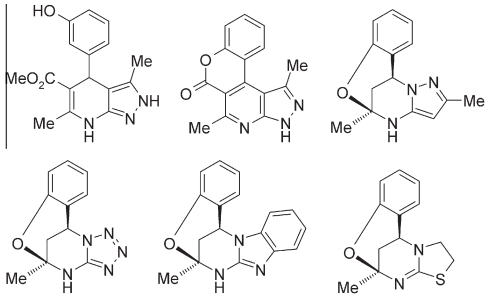
P2 = H, Me, Et, Pr, iPr, CH_2OH

A series of HIV-1 protease inhibitors containing an epsilon substituted lysinol backbone was synthesized. Two novel synthetic routes using *N*-boc-L-glutamic acid alpha-benzyl ester and 2,6-diaminopimelic acid were developed. Incorporation of this epsilon substituent enabled access to the S2 pocket of the enzyme, affording high potency inhibitors. Modeling studies and synthetic efforts suggest the potency increase is due to both conformational bias and van der Waals interactions with the S2 pocket.

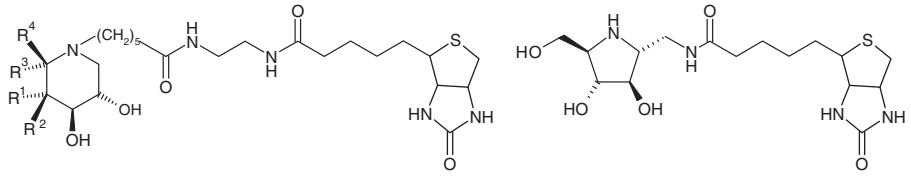
Structure–activity relationships and hepatic safety risks of thiazole agonists of the thrombopoietin receptor **pp 4069–4072**
Amy S. Antipas, Laura C. Blumberg, William H. Brissette, Matthew F. Brown, Jeffrey M. Casavant, Jonathan L. Doty, James Driscoll, Thomas M. Harris, Christopher S. Jones, Sandra P. McCurdy, Eric McElroy, Mark Mitton-Fry*, Michael J. Munchhof, David A. Reim, Lawrence A. Reiter, Sharon L. Ripp, Andrei Shavnya, Marc I. Smeets, Kristen A. Trevena



Monastrol analogs: A synthesis of pyrazolopyridine, benzopyranopyrazolopyridine, and oxygen-bridged azolopyrimidine derivatives and their biological screening **pp 4073–4076**
Jan Svetlik*, Lucia Veizerová, Thomas U. Mayer, Mario Catarinella



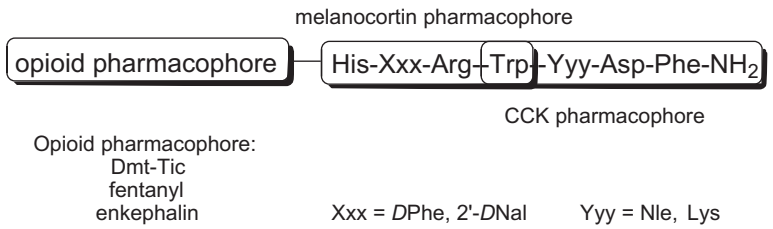
Synthesis and biological evaluation of novel biotin–iminoalditol conjugates **pp 4077–4079**
Gerit Pototschnig, Christian Morales De Csáky, Jose R. Montenegro Burke, Georg Schitter, Arnold E. Stütz, Chris A. Tarling, Stephen G. Withers, Tanja M. Wrodnigg*



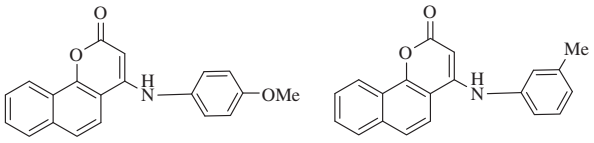
D-*gluco*: R^1 = OH, R^2 = H, R^3 = H, R^4 = CH_2OH
D-*galacto*: R^1 = H, R^2 = OH, R^3 = H, R^4 = CH_2OH
L-*ido*: R^1 = OH, R^2 = H, R^3 = CH_2OH, R^4 = H

The syntheses and biological evaluation of biotin–iminoalditol conjugates with D-*gluco*, L-*ido*, D-*galacto* configurations as well as of 2,5-dideoxy-2,5-imino-D-mannitol are reported.

Design and synthesis of trivalent ligands targeting opioid, cholecystokinin, and melanocortin receptors for the treatment of pain **pp 4080–4084**
Yeon Sun Lee, Steve Fernandes, Vinod Kulkarani, Alexander Mayorov, Peg Davis, Shou-wu Ma, Kathy Brown, Robert J. Gillies, Josephine Lai, Frank Porreca, Victor J. Hruby*

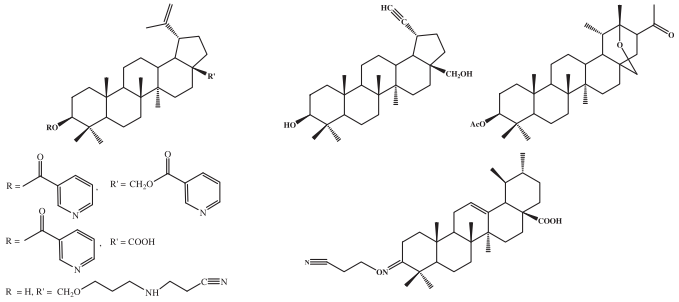


Antitumor agents 278. 4-Amino-2*H*-benzo[*h*]chromen-2-one (ABO) analogs as potent in vitro anti-cancer agents **pp 4085–4087**
Yizhou Dong, Kyoko Nakagawa-Goto, Chin-Yu Lai, Susan L. Morris-Natschke, Kenneth F. Bastow, Kuo-Hsiung Lee*

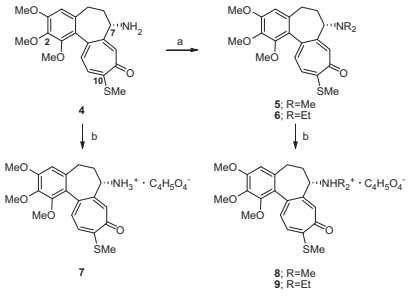


18 **24**

Betulin and ursolic acid synthetic derivatives as inhibitors of Papilloma virus **pp 4088–4090**
Oxana B. Kazakova*, Gul'nara V. Giniyatullina, Emil Yu. Yamansarov, Genrikh A. Tolstikov

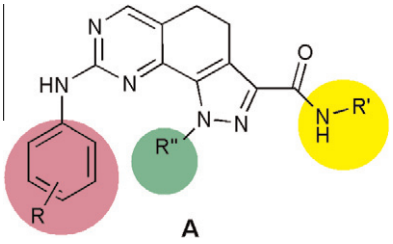


Antitumor agents 273. Design and synthesis of *N*-alkyl-thiocolchicinoids as potential antitumor agents **pp 4091–4094**
Takashi Kozaka, Kyoko Nakagawa-Goto, Qian Shi, Chin-Yu Lai, Ernest Hamel, Kenneth F. Bastow, Arnold Brossi, Kuo-Hsiung Lee*



4 **5**; R=Me **6**; R=Et **7** **8**; R=Me **9**; R=Et

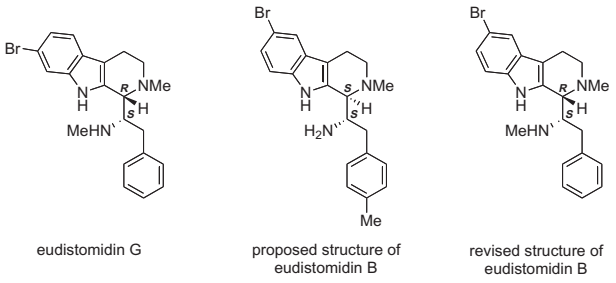
Structure-based optimization of potent PDK1 inhibitors **pp 4095–4099**
Mauro Angiolini*, Patrizia Banfi, Elena Casale, Francesco Casuscelli, Claudio Fiorelli, Maria B. Saccardo, Marco Silvagni, Fabio Zuccotto



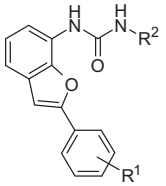
A

The design, synthesis, and X-ray crystal structures of potent dihydro-pyrazoloquinazolines PDK1 inhibitors having general formula A are reported.

Eudistomidin G, a new β-carboline alkaloid from the Okinawan marine tunicate *Eudistoma glaucus* and structure revision of eudistomidin B **pp 4100–4103**
Yohei Takahashi, Haruaki Ishiyama, Takaaki Kubota, Jun'ichi Kobayashi*

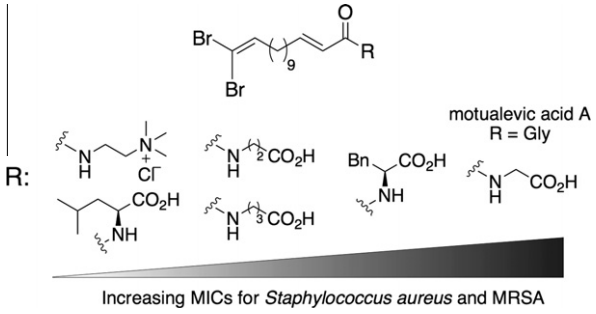


Benzofuran-substituted urea derivatives as novel P2Y$_1$ receptor antagonists **pp 4104–4107**
Reema K. Thalji*, Nambi Aiyar, Elizabeth A. Davenport, Joseph A. Erhardt, Lorena A. Kallal, Dwight M. Morrow, Shobha Senadhi, Cynthia L. Burns-Kurtis, Joseph P. Marino Jr.

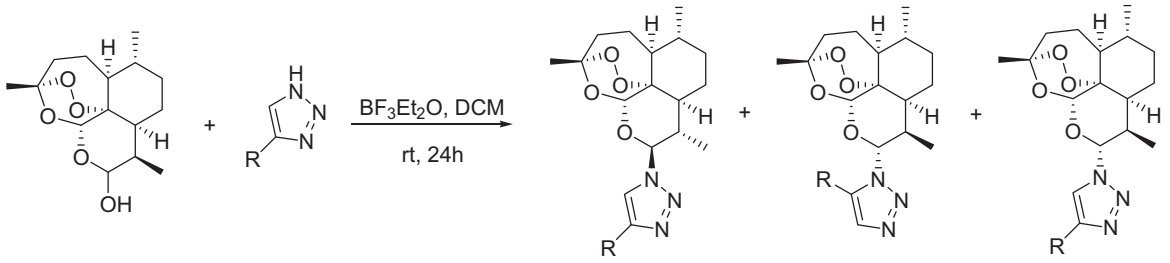


Benzofuran-substituted urea analogs have been identified as novel P2Y$_1$ receptor antagonists. Structure–activity relationship studies around the urea and the benzofuran moieties resulted in compounds having improved potency. Several analogs were shown to inhibit ADP-mediated platelet activation.

Motualevic acids and analogs: Synthesis and antimicrobial structure–activity relationships **pp 4108–4111**
Pradeep Cheruku, Jessica L. Keffer, Cajetan Dogo-Isonagie, Carole A. Bewley*



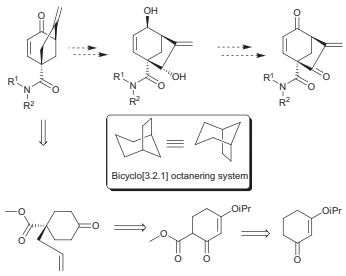
Acid-catalyzed synthesis of 10-substituted triazolyl artemisinins and their growth inhibitory activity against various cancer cells **pp 4112–4115**
Sangtae Oh, Woon-Seob Shin, Jungyeob Ham*, Seokjoon Lee*



Recombination of diterpenoid structure units: Synthesis of antitumor amides bearing functionalized bicyclo[3.2.1]octane ring **pp 4116–4119**

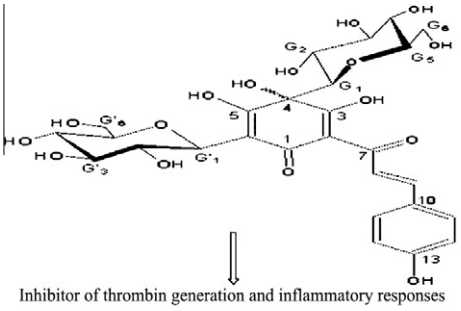
Zewei Mao, Yan Li, Jingbo Chen, Yuanyuan Wang, Hongbin Zhang*

In this work, 23 new amides (**14–36**) bearing a representative diterpenoid structure unit, the functionalized bicyclo[3.2.1]octane ring, have been synthesized and its antitumor potential is studied. In vitro studies demonstrate that a number of amides with the bicyclo[3.2.1]oct-3-en-2-one subunit are active against HL-60, SMMC-7721, A-549, SK-BR-3, and PANC-1 tumor cell lines. The hybrid derivative, compound **20**, was found to be the most potent compound (IC_{50} = 1.05 μM against HL-60) and more active than cisplatin (DDP), the positive control. Additionally, compound **20** exhibited broad spectrum in vitro anticancer activity with IC_{50} values of 1.1–4.3 μM against the five tested cancer cell lines.



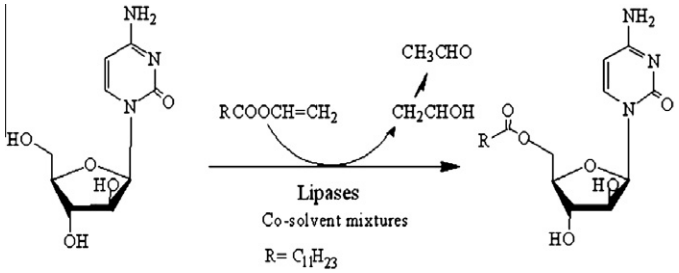
Hydroxysafflor Yellow A suppresses thrombin generation and inflammatory responses following focal cerebral ischemia–reperfusion in rats **pp 4120–4124**

Xia Sun, Xinbing Wei, Sifeng Qu, Yunxue Zhao, Xiumei Zhang*



Efficient synthesis of 5′-*O*-laurate of 1-β-D-arabinofuranosylcytosine via highly regioselective enzymatic acylation in binary solvent mixtures **pp 4125–4127**

Xiao-feng Li, Min-hua Zong, Guang-lei Zhao*

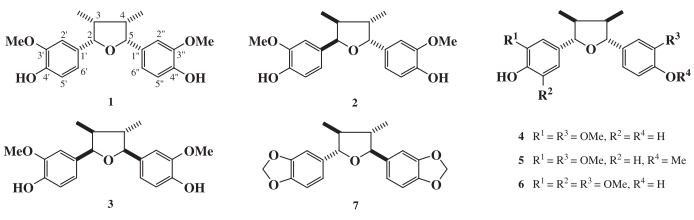


Regioselective 5′-acylation of ara-C with VL by lipase was explored in organic solvents. And the effects of several crucial factors influencing the enzymatic acylation of ara-C were also systematically examined.

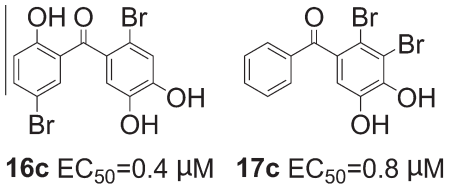
AMP-activated protein kinase (AMPK) activators from *Myristica fragrans* (nutmeg) and their anti-obesity effect **pp 4128–4131**

Phi Hung Nguyen, Thi Van Thu Le, Hu Won Kang, Jooyoung Chae, Sang Kyum Kim, Kwang-il Kwon, Dae Bang Seo, Sang Jun Lee, Won Keun Oh*

In our program to search new AMPK activators from plants, seven 2,5-bis-aryl-3,4-dimethyltetrahydrofuran lignans, tetrahydrofuroguaiacin B (**1**), saucernetindiol (**2**), verrucosin (**3**), nectandrin B (**4**), nectandrin A (**5**), fragransin C_1 (**6**), and galbacin (**7**) were isolated from *Myristica fragrans* (nutmeg). Among the isolates, compounds **1**, **4**, and **5** at 5 μM produced strong AMPK stimulation in differentiated C2C12 cells. The active fraction containing of high content of nectandrin B showed protective effect on the increase of blood glucose and body weight in high-fat diet (HFD)-induced mice.



Synthesis and biological activity of halophenols as potent antioxidant and cytoprotective agents **pp 4132–4134**
Wanyi Zhao, Xiue Feng, Shurong Ban, Wenhan Lin, Qingshan Li*

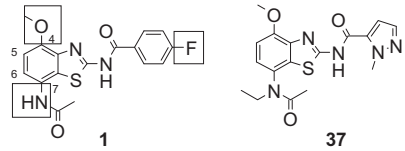


A variety of halophenols were prepared by a practical route. The halophenols all displayed promising DPPH radical-scavenging activity, and two bromophenols exhibited high protective activity against H_2O_2-induced injury in HUVEC.

An analysis of the 'legal high' mephedrone **pp 4135–4139**
Simon Gibbons*, Mire Zloh

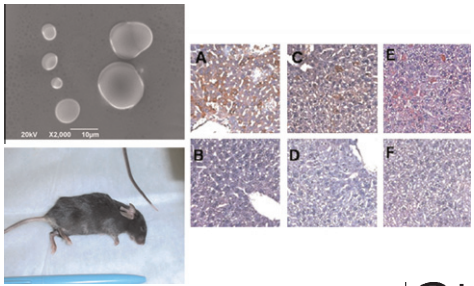
Analysis of a sample of the methyl-cathinone derivative mephedrone (**1**) has led to the full unambiguous assignment of the spectral data for this compound. Molecular modelling indicated that the methyl-cathinone series are more hydrophilic and planar than the methyl-amphetamines and these properties may in part explain the toxicity of this drug of abuse.

4-Substituted-7-*N*-alkyl-*N*-acetyl 2-aminobenzothiazole amides: Drug-like and non-xanthine based A_{2B} adenosine receptor antagonists **pp 4140–4146**
Adrian Wai-Hing Cheung*, John Brinkman, Fariborz Firooznia, Alexander Flohr, Joseph Grimsby, Mary Lou Gubler, Kevin Guertin, Rachid Hamid, Nicholas Marcopulos, Roger D. Norcross, Lida Qi, Gwendolyn Ramsey, Jenny Tan, Yang Wen, Ramakanth Sarabu



7-*N*-Acetamide-4-methoxy-2-aminobenzothiazole 4-fluorobenzamide (compound **1**) was chosen as a drug-like and non-xanthine based starting point for the discovery of A_{2B} receptor antagonists because of its slight selectivity against A_1 and A_{2A} receptors and modest A_{2B} potency. SAR exploration of compound **1** described herein included modifications to the 7-*N*-acetamide group, substitution of the 4-methoxy group by halogens as well as replacement of the *p*-flouro-benzamide side chain. This work culminated in the identification of compound **37** with excellent A_{2B} potency, modest selectivity versus A_{2A} and A_1 receptors, and good rodent PK properties.

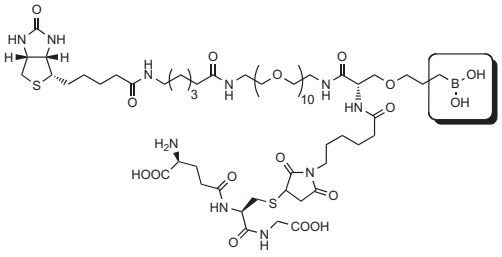
Synthesis, characterization and preliminary analysis of in vivo biological activity of chitosan/celecoxib microcapsules **pp 4147–4151**
Shuk-Yan Cheng, Marcus Chun-Wah Yuen, Pik-Ling Lam, Roberto Gambari, Raymond Siu-Ming Wong, Gregory Yin-Ming Cheng, Paul Bo-San Lai, See-Wai Tong, Kit-Wah Chan, Fung-Yi Lau, Stanton Hon-Lung Kok*, Kim-Hung Lam*, Chung-Hin Chui*



Mice with orally administrated chitosan/celecoxib microcapsules showed a better inhibition of cyclooxygenase-2 protein expression in the hepatocytes when compared with those of vehicle control and simple oral administration of celecoxib.

Probe molecule equipped with boronic acid moiety as a reversible cross-linking group improves its binding affinity **pp 4152–4155**

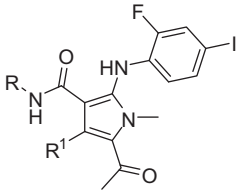
Naoyuki Kotoku, Xiu-Han Guo, Masayoshi Arai, Motomasa Kobayashi*



The presence of boronic acid moiety in an appropriate position enhances binding affinity of probe molecule toward its target protein, probably by forming a reversible cross-link.

Structure-based design and synthesis of pyrrole derivatives as MEK inhibitors **pp 4156–4158**

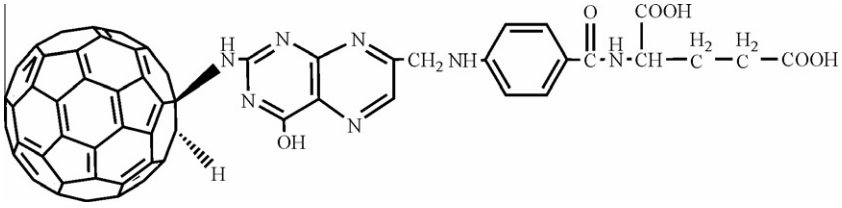
Michael B. Wallace*, Mark E. Adams, Toufike Kanouni, Clifford D. Mol, Douglas R. Dougan, Victoria A. Feher, Shawn M. O'Connell, Lihong Shi, Petro Halkowycz, Qing Dong



A series of potent pyrrole-based inhibitors of MEK kinase was designed and synthesized. Structural properties and biological activities are described.

Folacin C_{60} derivative exerts a protective activity against oxidative stress-induced apoptosis in rat pheochromocytoma cells **pp 4159–4162**

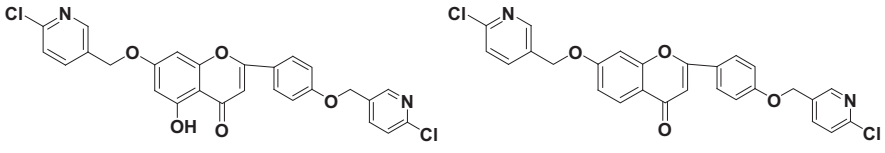
Zhen Hu*, Wenchao Guan, Wei Wang, Zhou Zhu, Yanhong Wang



Folacin C_{60} derivative has been synthesised and characterized in our recent research. As a novel derivative of C_{60}, the folacin C_{60} derivative is soluble in H_2O which behaves as a free radical scavenger. Rat pheochromocytoma cells treated with hydrogen peroxide underwent cytotoxicity and apoptotic death is determined by MTT assay and flow cytometry analysis. The results suggest that folacin C_{60} derivative has the potential to prevent oxidative stress-induced cell death without evident toxicity.

Synthesis and molecular docking studies of novel 2-chloro-pyridine derivatives containing flavone moieties as potential antitumor agents **pp 4163–4167**

Xin-Hua Liu, Hui-Feng Liu, Xu Shen, Bao-An Song, Pinaki S. Bhadury, Hai-Liang Zhu*, Jin-Xing Liu, Xing-Bao Qi



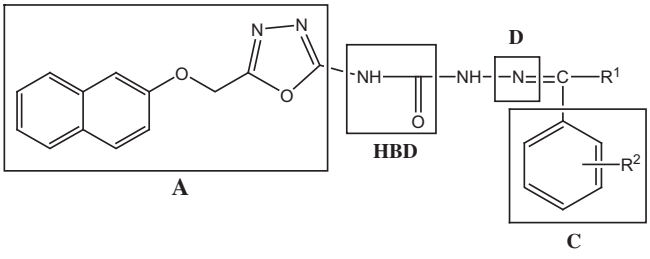
6e **6f**

The bioassay tests showed that compounds **6e** and **6f** exhibited certain effective against gastric SGC-7901 cell with the IC_{50} values were 22.28 ± 6.26 and 18.45 ± 2.79 μg/mL, respectively. Compound **6e** can strongly inhibit telomerase with IC_{50} value of 0.8 ± 0.07 μg/mL. The docking simulation result shows that some 2-chloro-pyridine containing flavone (**6e**) can combine well with the telomerase active site may use as potential telomerase inhibitors.

Novel semicarbazones based 2,5-disubstituted-1,3,4-oxadiazoles: One more step towards establishing four binding site pharmacophoric model hypothesis for anticonvulsant activity **pp 4168–4172**

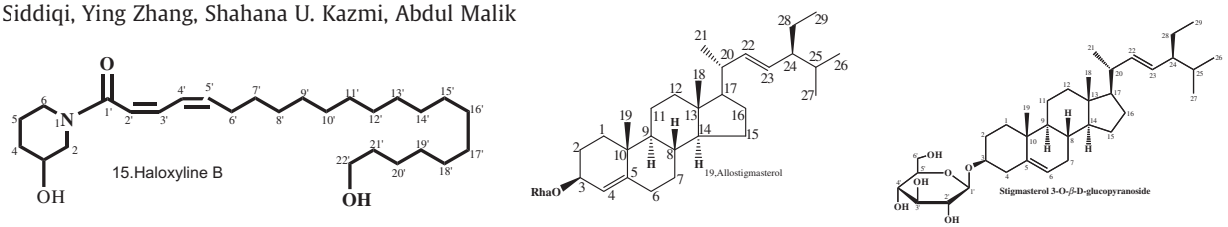
Harish Rajak*, Ravitas Deshmukh, Ravichandran Veerasamy, Ajay Kumar Sharma, Pradeep Mishra, Murli Dhar Kharya

A series of novel semicarbazones based 2,5-disubstituted-1,3,4-oxadiazoles possessing four vital structural features (A) hydrophobic aryl ring system, (HBD) hydrogen binding domain, (D) electron donor moiety and (C) distal aryl ring required for anticonvulsant activity are disclosed. The aryl semicarbazones have been found to possess anticonvulsant activity through GABA mediation.



In vitro antituberculosis activities of the constituents isolated from *Haloxylon salicornicum* **pp 4173–4176**

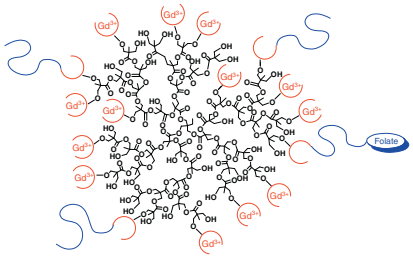
Nazia Bibi, Sheraz Ahmad. K. Tanoli, Sadia Farheen*, Nighat Afza, Salman Siddiqi, Ying Zhang, Shahana U. Kazmi, Abdul Malik



In vitro antituberculosis activities of series of four fractions and twenty (**1**–**20**) pure compounds included seven triterpenes, two alkaloids, two cycloheximide derivatives, two coumarins six sterol derivatives and a long chain alcohol, respectively, isolated from *Haloxylon salicornicum* were evaluated against *Mycobecterium tuberculosis* H37Rv. Actively growing cultures were tested by rapid colorimetric method while the stationary phase cultures were tested by drug exposure methods for bactericidal activity. The MIC values were found significant (50 μg/ml) for the compounds **15**, **19** and **20** where as rest of the compounds invariably showed MIC value of 100 μg/ml against the logarithmic phase culture, these were compare to Isoniazid as control drug.

Synthesis and characterization of multifunctional hyperbranched polyesters as prospective contrast agents for targeted MRI **pp 4177–4181**

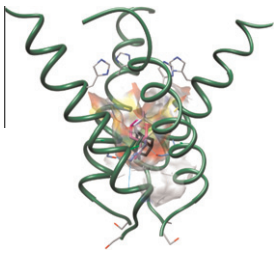
Zili Sideratou*, Dimitris Tsiourvas, Theodossis Theodossiou, Michael Fardis, Constantinos M. Paleos



Hyperbranched aliphatic polyesters bearing gadolinium chelate moieties, a protective PEG-coating and a folate targeting ligand were prepared affording non-toxic biodegradable nanocarriers of enhanced water relaxivity values and cell specificity.

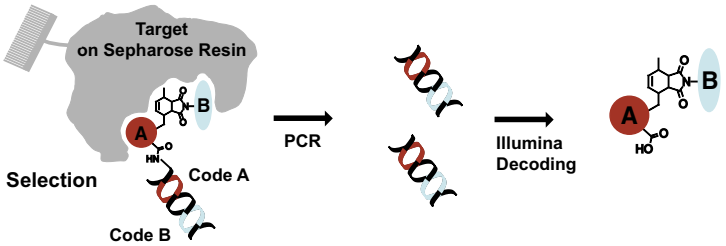
Interaction of aminoadamantane derivatives with the influenza A virus M2 channel-Docking using a pore blocking model **pp 4182–4187**

Stelios Eleftheratos, Philip Spearpoint, Gabriella Ortore, Antonios Kolocouris*, Adriano Martinelli, Stephen Martin, Alan Hay



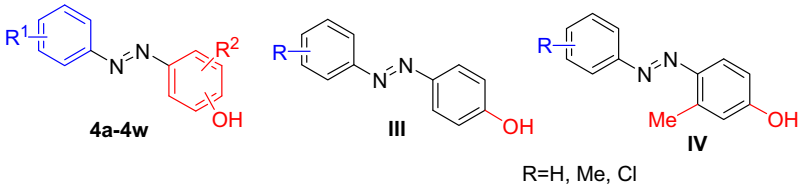
Binding affinity changes for a series of synthetic aminoadamantane ligands to influenza virus A M2 protein are qualitatively described from docking calculations on M2TM using a pore blocking model.

High-throughput sequencing for the identification of binding molecules from DNA-encoded chemical libraries **pp 4188–4192**
Fabian Buller, Martina Steiner, Jörg Scheuermann, Luca Mannocci, Ina Nissen, Manuel Kohler, Christian Beisel, Dario Neri*



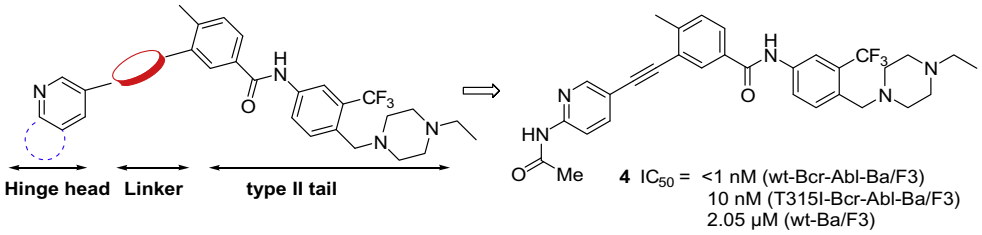
DNA-encoded chemical libraries are large collections of small organic molecules, individually coupled to DNA fragments that serve as amplifiable identification bar codes. The isolation of specific binders requires a quantitative analysis of the distribution of DNA fragments in the library before and after selection. Here, we show how Illumina sequencing can be applied to the analysis of DNA-encoded chemical libraries.

Synthesis of diaryl-azo derivatives as potential antifungal agents **pp 4193–4195**
Hui Xu*, Xiwen Zeng



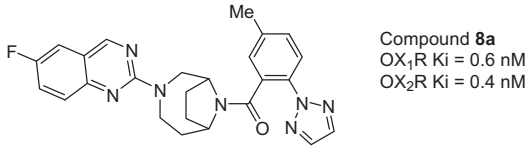
Among of all the compounds **4a**–**w**, 4-((un)substituted phenylazo)-phenol (**III**) and 4-((un)substituted phenylazo)-3-methylphenol (**IV**) might be considered as new promising lead candidates for further design and synthesis of agricultural fungicides.

Broad spectrum alkynyl inhibitors of T315I Bcr-Abl **pp 4196–4200**
Xianming Deng, Sang Min Lim, Jianming Zhang, Nathanael S. Gray*



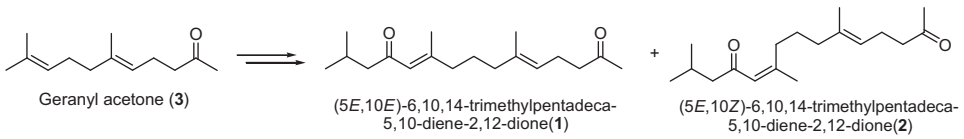
A series of alkyne-containing type II inhibitors with potent inhibitory activity of T315I Bcr-Abl has been identified. The most active compound **4** exhibits an EC_{50} of less than 1 nM against wild-type Bcr-Abl and an EC_{50} of 10 nM against T315I mutant but is broadly active against a number of other kinases.

Discovery of 3,9-diazabicyclo[4.2.1]nonanes as potent dual orexin receptor antagonists with sleep-promoting activity in the rat **pp 4201–4205**
Paul J. Coleman*, John D. Schreier, Anthony J. Roecker, Swati P. Mercer, Georgia B. McGaughey, Christopher D. Cox, George D. Hartman, C. Meacham Harrell, Duane R. Reiss, Scott M. Doran, Susan L. Garson, Wayne B. Anderson, Cuyue Tang, Thomayant Prueksaritanont, Christopher J. Winrow, John J. Renger

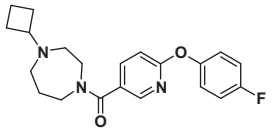


In this Letter, we describe the synthesis of constrained diazepanes including 3,9-diazabicyclo[4.2.1]nonane **8a** that has improved oral bioavailability and sleep-promoting activity in a rat EEG model.

Synthesis of two marine farnesylacetones that dilate the basilar arteries of rabbits **pp 4206–4209**
Sangtae Oh, Byong-Gon Park, Jungyeob Ham, Seokjoon Lee*

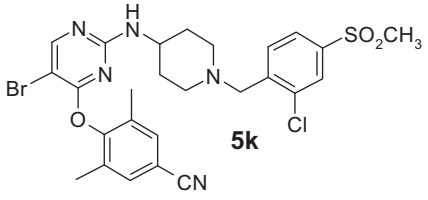


Pre-clinical characterization of aryloxypyridine amides as histamine H_3 receptor antagonists: Identification of candidates for clinical development **pp 4210–4214**
Michael A. Letavic*, Leah Aluisio, John R. Atack, Pascal Bonaventure, Nicholas I. Carruthers, Christine Dugovic, Anita Everson, Mark A. Feinstein, Ian C. Fraser, Kenway Hoey, Xiaohui Jiang, John M. Keith, Tatiana Koudriakova, Perry Leung, Brian Lord, Timothy W. Lovenberg, Kiev S. Ly, Kirsten L. Morton, S. Timothy Motley, Diane Nepomuceno, Michele Rizzolio, Raymond Rynberg, Kia Sepassi, Jonathan Shelton

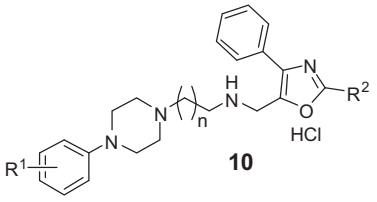


Novel aryloxypyridines are high affinity histamine H_3 antagonists.

Discovery of piperidin-4-yl-aminopyrimidines as HIV-1 reverse transcriptase inhibitors. *N*-Benzyl derivatives with broad potency against resistant mutant viruses **pp 4215–4218**
Denis J. Kertesz*, Christine Brotherton-Pleiss, Minmin Yang, Zhanguo Wang, Xianfeng Lin, Zongxing Qiu, Donald R. Hirschfeld, Shelley Gleason, Taraneh Mirzadegan, Pete W. Dunten, Seth F. Harris, Armando G. Villaseñor, Julie Qi Hang, Gabrielle M. Heilek, Klaus Klumpp

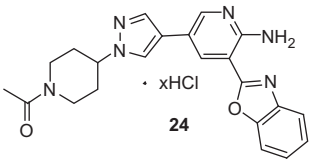


Synthesis and biological evaluation of oxazole derivatives as T-type calcium channel blockers **pp 4219–4222**
Jie Eun Lee, Hun Yeong Koh, Seon Hee Seo, Yi Yeon Baek, Hyewhon Rhim, Yong Seo Cho, Hyunah Choo*, Ae Nim Pae*



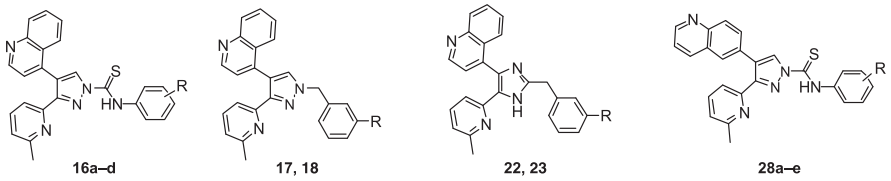
Oxazole derivatives as T-type calcium channel blockers were synthesized and their biological results were reported.

Discovery of aminopyridines substituted with benzoxazole as orally active c-Met kinase inhibitors **pp 4223–4227**
Sung Yun Cho, Sun-Young Han, Jae Du Ha, Jae Wook Ryu, Chong Ock Lee, Heejung Jung, Nam Sook Kang, Hyoung Rae Kim, Jong Sung Koh, Jongkook Lee*



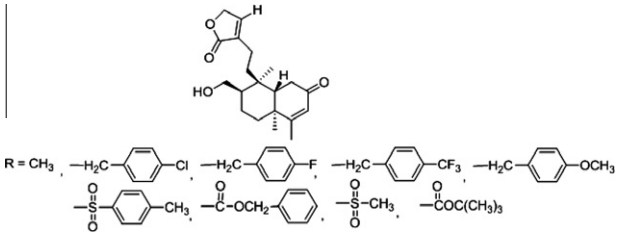
A series of aminopyridines substituted with benzoxazole were designed and synthesized as very potent c-Met kinase inhibitors.

Synthesis and biological evaluation of 2-pyridyl-substituted pyrazoles and imidazoles as transforming growth factor-β type 1 receptor kinase inhibitors **pp 4228–4232**
Purushottam M. Dewang, Dae-Kee Kim*



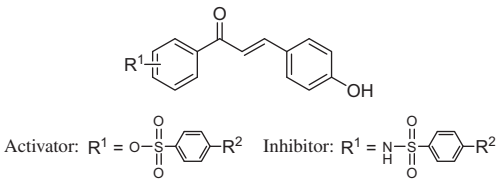
Synthesis of a new series of 2-pyridyl-substituted pyrazoles and imidazoles as ALK5 inhibitors is described.

In vitro and in vivo antimalarial evaluation of semi-synthetic derivatives of gomphostenin **pp 4233–4236**
Manisha Sathe, M. P. Kaushik*



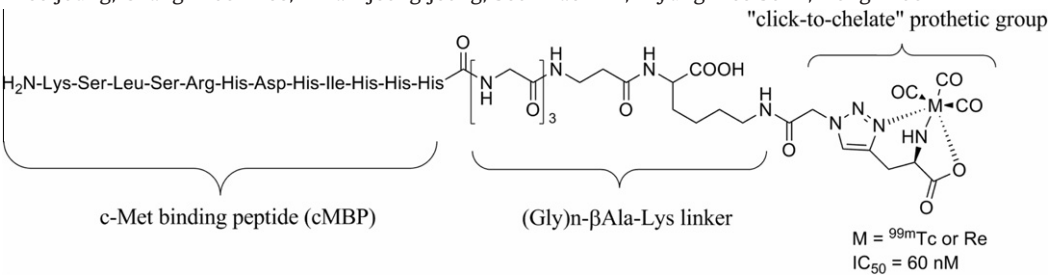
A novel series of semi-synthetic gomphostenin derivatives (1 to 9) were prepared utilizing C-14 hydroxyl group for the first time and studied for their antimalarial properties. In vitro antiplasmodial activity was evaluated against both the chloroquine-sensitive and resistant strains of *Plasmodium falciparum*. Most of the compounds exhibited superior or comparable antiplasmodial activity compared to parent compound i.e. gomphostenin (GN). Based upon in vitro antiplasmodial activity, compounds with IC_{50} values less than 10 μM were selected for in vivo antiplasmodial evaluation against *Plasmodium berghei* infection in mice model. GN derivatives 3 and 5 were found to have curative activity with moderate chemosupression of 65% and 69% respectively at the dose level of 150 mg/kg/day.

Chemoselective regulation of TREK2 channel: Activation by sulfonate chalcones and inhibition by sulfonamide chalcones **pp 4237–4239**
Eun-Jin Kim, Hyung Won Ryu, Marcus J. Curtis-Long, Jaehee Han, Jun Young Kim, Jung Keun Cho, Dawon Kang*, Ki Hun Park*



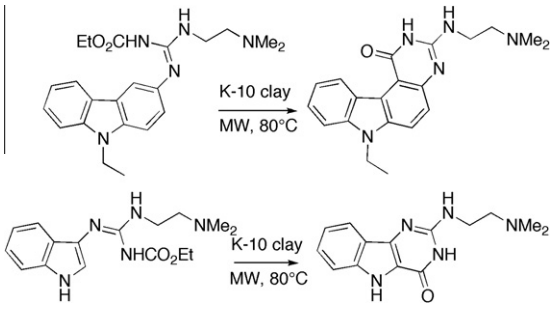
The sulfonamide chalcones behaved as inhibitor, whereas the sulfonate analogues activated TREK2.

Synthesis of Tc-99m labeled 1,2,3-triazole-4-yl c-met binding peptide as a potential c-met receptor kinase positive tumor imaging agent **pp 4240–4243**
Eun-Mi Kim, Min-Hee Joung, Chang-Moon Lee, Hwan-Jeong Jeong, Seok Tae Lim, Myung-Hee Sohn, Dong Wook Kim*

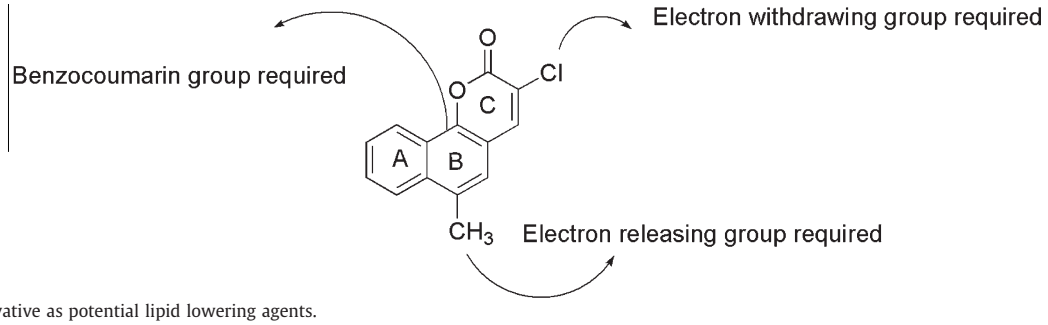


Tc-99m labeled 1,2,3-triazole-4-yl c-Met binding peptide (cMBP), as a potential c-Met receptor kinase positive tumor imaging agent, were prepared by solid phase peptide synthesis and the 'click-to-chelate' protocol.

Montmorillonite K-10 catalyzed cyclization of *N*-ethoxycarbonyl-*N*′-arylguanidines: Access to pyrimido[4,5-*c*]carbazole and pyrimido[5,4-*b*]indole derivatives **pp 4244–4247**
Julien Debray, Walid Zeghida, Brigitte Baldeyrou, Christine Mahieu, Amélie Lansiaux, Martine Demeunynck*

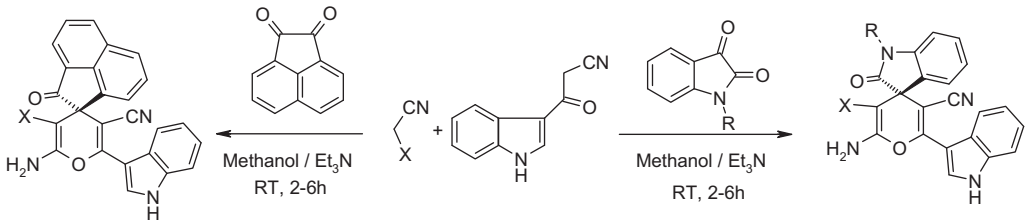


Novel coumarin derivatives as potential antidyslipidemic agents **pp 4248–4251**
Koneni V. Sashidhara*, Abdhesh Kumar, Manoj Kumar, Ravi Sonkar, Gitika Bhatia, A. K. Khanna



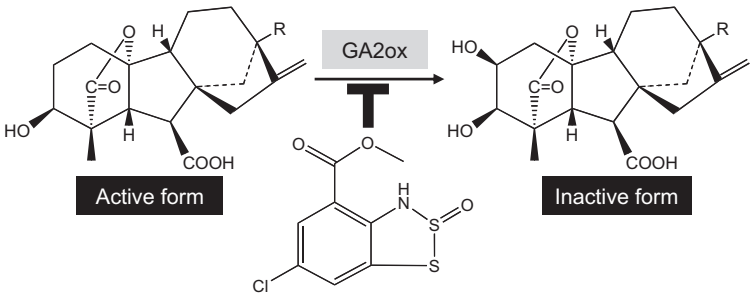
Novel coumarin derivative as potential lipid lowering agents.

One-pot multicomponent synthesis and anti-microbial evaluation of 2′-(indol-3-yl)-2-oxospiro(indoline-3,4′-pyran) derivatives **pp 4252–4258**
A. Nandakumar, Prakasam Thirumurugan, Paramasivan T. Perumal*, P. Vembu, M. N. Ponnuswamy, P. Ramesh

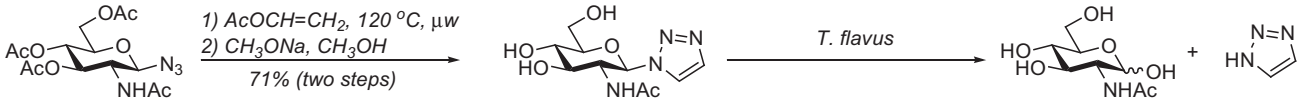


A simple and efficient method for the one-pot three-component synthesis of new spirooxindoles in room temperature is described. The newly synthesize spirooxindoles were screened for anti-microbial activity and the results are good on comparison with of standard antibacterial compounds.

Screening and characterization of an inhibitory chemical specific to Arabidopsis gibberellin 2-oxidases **pp 4259–4262**
Masato Otani, Jung-Min Yoon, Seung-Hyun Park, Tadao Asami, Masatoshi Nakajima*

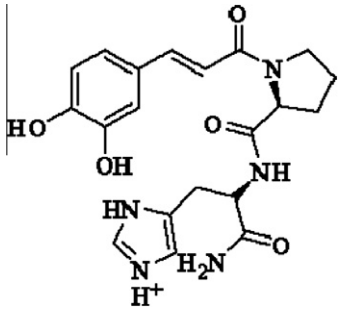


Synthesis and biological activity of glycosyl-1*H*-1,2,3-triazoles **pp 4263–4265**
Kristýna Slámová, Petr Marhol, Karel Bezouška, Lise Lindkvist, Signe G. Hansen, Vladimír Křen*, Henrik H. Jensen*



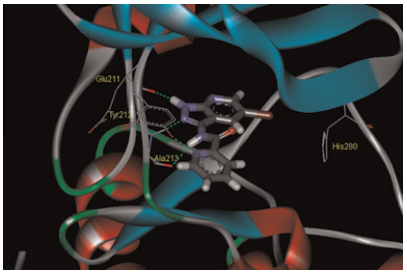
Activator of natural killer lymphocytes

Antioxidative activities of histidine containing caffeic acid-dipeptides **pp 4266–4272**
Hyo-Suk Seo, Seon-Yeong Kwak, Yoon-Sik Lee*



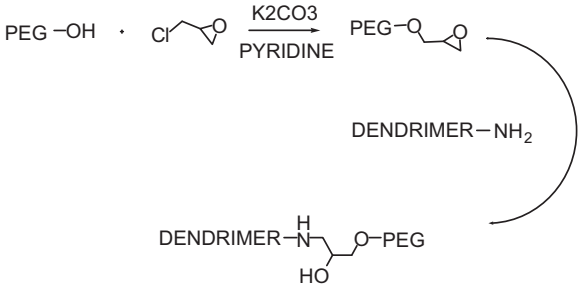
Caffeic acid (CA)-histidine containing dipeptide conjugates were synthesized to enhance antioxidative activity of CA. Among them, CA-Pro-His-NH_2 exhibited the strongest antioxidative activity.

Design and synthesis of 1,4,5,6-tetrahydropyrrolo[3,4-*c*]pyrazoles and pyrazolo[3,4-*b*]pyridines for Aurora-A kinase inhibitors **pp 4273–4278**
Jianyou Shi, Guobin Xu, Wei Zhu, Haoyu Ye, Shengyong Yang, Youfu Luo, Jing Han, Jincheng Yang, Rui Li*, Yuquan Wei, Lijuan Chen*



Pyrazolo[3,4-*b*]pyridines represented as a novel class of compounds to inhibit the Aurora-A's activity were synthesized and evaluated.

A new approach for PEGylation of dendrimers **pp 4279–4281**
Hemant Khambete, Surya P. Gautam, C. Karthikeyan, Suman Ramteke*, N. S. Hari Narayana Moorthy, Piyush Trivedi



In present work we have synthesized PEGylated polyamidoamine (PAMAM) dendrimers using epichlorhydrin as a linker. The PEGylated dendrimers were evaluated for color reaction UV, IR and NMR studies and compared with standard data.

OTHER CONTENT

Corrigendum **p 4282**

*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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