

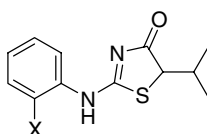
Contents

ARTICLES

The discovery of 2-anilinothiazolones as 11 β -HSD1 inhibitors

pp 6056–6061

Chester Yuan, David J. St. Jean, Jr., Qingyian Liu, Lynn Cai, Aiwen Li, Nianhe Han, George Moniz, Ben Askew, Randall W. Hungate, Lars Johansson, Lars Tedenborg, David Pyring, Meredith Williams, Clarence Hale, Michelle Chen, Rod Cupples, Jiandong Zhang, Steven Jordan, Michael D. Bartberger, Yaxiong Sun, Maurice Emery, Minghan Wang and Christopher Fotsch*



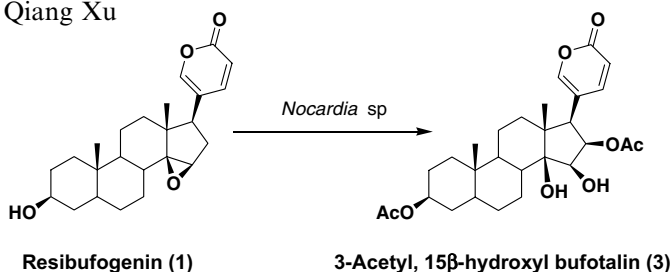
2, X = Cl, 11 β -HSD1 K_i = 7.2 nM
3, X = F, 11 β -HSD1 K_i = 17 nM

Microbial transformation of three bufadienolides by *Nocardia* sp. and some insight for the cytotoxic structure–activity relationship (SAR)

pp 6062–6065

Jian Zhang, Yang Sun, Ji-Hua Liu, Bo-Yang Yu* and Qiang Xu

Resibufogenin (1) was converted to a bufotalin derivate, 3-acetyl 15 β -hydroxyl bufotalin (3), by *Nocardia* sp. NRRL 5646 through a selective epoxy ring cleavage and a regio-selective acetoxylation, the product showed significantly increased cytotoxicities.

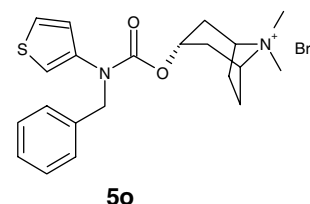


Discovery of novel 8-azoniabicyclo[3.2.1]octane carbamates as muscarinic acetylcholine receptor antagonists

pp 6066–6069

Dramane I. Lainé,* Haibo Xie, Noémie Buffet, James J. Foley, Peter Buckley, Edward F. Webb, Katherine L. Widdowson, Michael R. Palovich and Kristen E. Belmonte

In the course of our research program to develop novel muscarinic receptor antagonists for the treatment of COPD, new tropane carbamate derivatives were identified as potent anti-muscarinic agents. The synthesis, structure–activity relationships, and pharmacological evaluation that led to the identification of compound 50 are described.

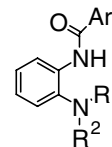


Potent 2'-aminoanilide inhibitors of cFMS as potential anti-inflammatory agents

pp 6070–6074

Raymond J. Patch, Benjamin M. Brandt, Davoud Asgari, Nand Baidur,
Naresh K. Chadha, Taxiarchis Georgiadis, Wing S. Cheung, Ioanna P. Petrounia,
Robert R. Donatelli, Margery A. Chaikin and Mark R. Player*

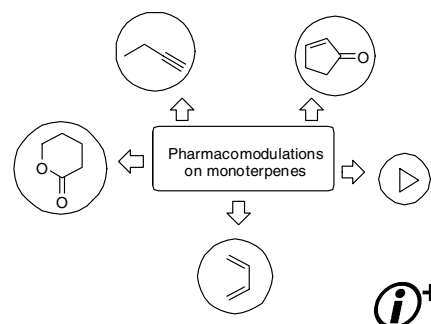
A series of 2'-aminoanilides have been identified which exhibit potent and selective inhibitory activity against the cFMS tyrosine kinase. Initial SAR studies within this series are described which examine aroyl and amino group substitutions, as well as the introduction of hydrophilic substituents on the benzene core. Compound **47** inhibits the isolated enzyme ($IC_{50} = 0.027 \mu M$) and blocks CSF-1-induced proliferation of bone marrow-derived macrophages ($IC_{50} = 0.11 \mu M$) and as such, serves as a lead candidate for further optimization studies.

**Modifications of the chemical structure of terpenes in antiplasmodial and antifungal drug research**

pp 6075–6078

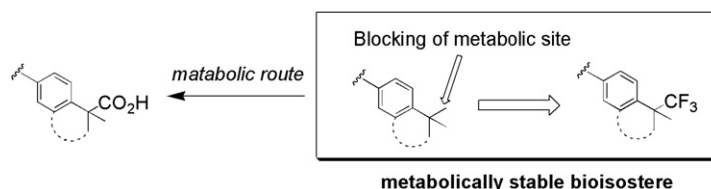
David Olnagier, Philippe Costes, Antoine Berry, Marie-Denise Linas, Martine Urrutigoity,
Odile Dechy-Cabaret and Françoise Benoit-Vical*

Various natural monoterpenes and new monoterpene derivatives, obtained through selective chemical reactions, present specific and promising antimalarial activity on *Plasmodium falciparum* but no activity against *Candida albicans*.

**Synthesis of aromatic compounds containing a 1,1-dialkyl-2-trifluoromethyl group, a bioisostere of the *tert*-alkyl moiety**

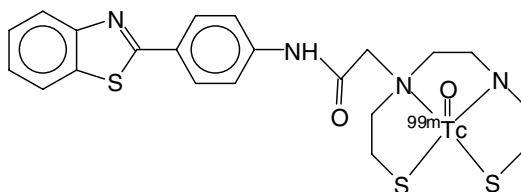
pp 6079–6085

Hiroataka Tanaka and Yuji Shishido*

**Synthesis and evaluation of a ^{99m}Tc -BAT-phenylbenzothiazole conjugate as a potential in vivo tracer for visualization of amyloid β**

pp 6086–6090

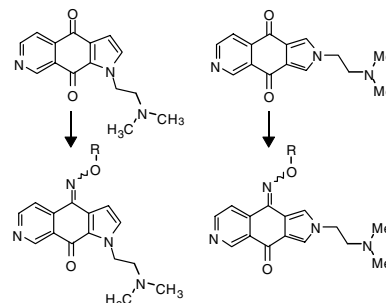
K. Serdons,* T. Verduyck, J. Cleynhens, C. Terwinghe, L. Mortelmans, G. Bormans and A. Verbruggen



A protected bis-amino-bis-thiol (BAT) tetraligand was conjugated with 2-(4'-aminophenyl)-1,3-benzothiazole, a derivative of thioflavin-T with known affinity for amyloid. The conjugate was efficiently labelled with ^{99m}Tc and biologically evaluated.

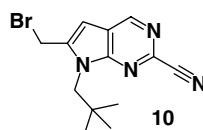
Synthesis and biological evaluation of novel cytotoxic azanaphthoquinone annelated pyrrolo oximes pp 6091–6095Karem Shanab, Nipawan Pongprom, Eva Wulz, Wolfgang Holzer, Helmut Spreitzer,*
Peter Schmidt, Babette Aicher, Gilbert Müller and Eckhard Günther

Two novel series of azanaphthoquinone annelated pyrrolo oximes were synthesized by aza-condensation. The cytotoxic evaluation on different cancer cell lines is reported and discussed comparing these two isomers.

**Novel scaffold for cathepsin K inhibitors**

pp 6096–6100

Naoki Teno,* Takahiro Miyake, Takeru Ehara, Osamu Irie, Junichi Sakaki, Osamu Ohmori, Hiroki Gunji, Naoko Matsuura, Keiichi Masuya, Yuko Hitomi, Kazuhiko Nonomura, Miyuki Horiuchi, Keigo Gohda, Atsuko Iwasaki, Ichiro Umemura, Sachiyo Tada, Motohiko Kometani, Genji Iwasaki, Sandra W. Cowan-Jacob, Martin Missbach, René Lattmann and Claudia Betschart

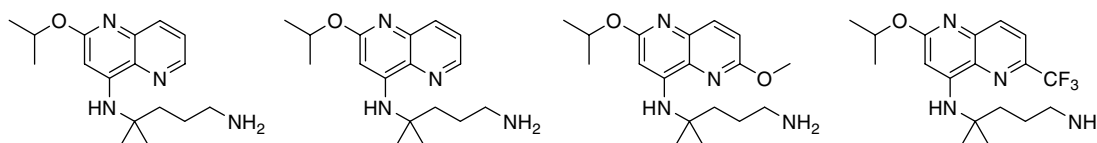


Pyrrolopyrimidine, a novel scaffold, allows to adjust interactions within the S3 subsite of cathepsin K. The core intermediate **10** facilitated the P3 optimization and identified highly potent and selective cathepsin K inhibitors.

Synthesis and evaluation of naphthyridine compounds as antimalarial agents

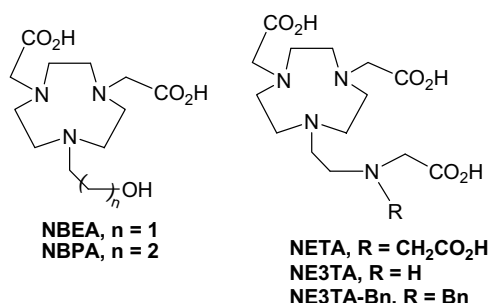
pp 6101–6106

Shuren Zhu,* Quan Zhang, Chandrashekar Gudise, Li Meng, Lai Wei, Erika Smith and Yuliang Kong

**Novel synthetic ligands for targeted PET imaging and radiotherapy of copper**

pp 6107–6110

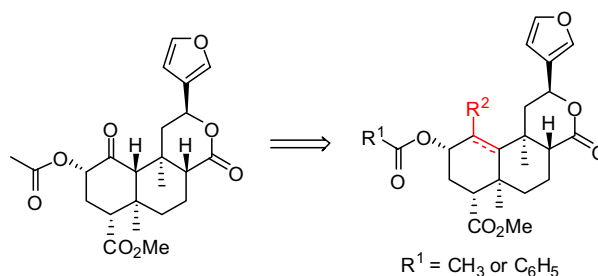
Hyun-Soon Chong,* Santosh Mhaske, Mai Lin, Sankar Bhuniya, Hyun A. Song, Martin W. Brechbiel and Xiankai Sun



Synthetic studies of neoclerodane diterpenes from *Salvia divinorum*: Exploration of the 1-position

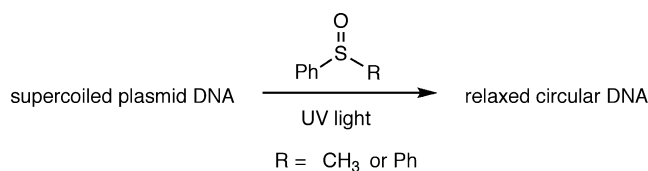
pp 6111–6115

Kenneth G. Holden, Kevin Tidgewell, Alfred Marquam, Richard B. Rothman, Hernán Navarro and Thomas E. Prisinzano*

**DNA cleavage by photolysis of aryl sulfoxides**

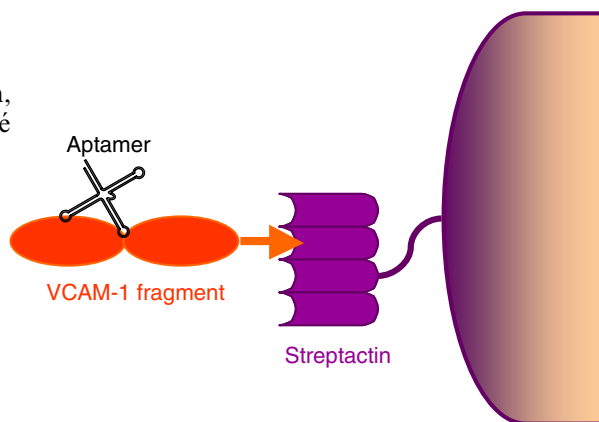
pp 6116–6118

Daniel J. Mayo, David P. Turner, Beth E. Zucconi and Allison H. Predecki*

**Binding of an aptamer to the N-terminal fragment of VCAM-1**

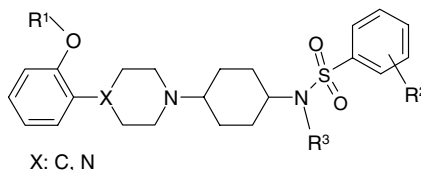
pp 6119–6122

Fabien Chauveau, Youssef Aissouni, Jorg Hamm, Hervé Boutin, Domenico Libri, Frédéric Ducongé and Bertrand Tavitian*

**Aminocyclohexylsulfonamides: Discovery of metabolically stable $\alpha_{1a/1d}$ -selective adrenergic receptor antagonists for the treatment of benign prostatic hyperplasia/lower urinary tract symptoms (BPH/LUTS)**

pp 6123–6128

George Chiu,* Shengjian Li, Hong Cai, Peter J. Connolly, Sean Peng, Kathe Stauber, Virginia Pulito, Jingchun Liu and Steven A. Middleton

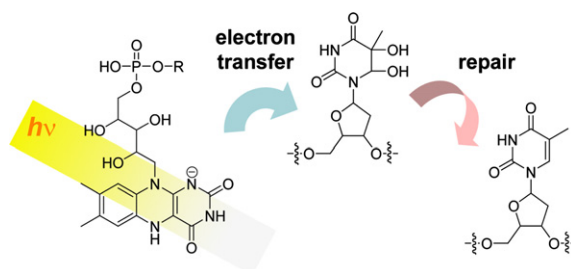


A series of aminocyclohexylsulfonamides that show selectivity to human $\alpha_{1a/1d}$ adrenergic receptors and are stable against human liver microsomal metabolism were developed. These compounds have potential for the treatment of BPH/LUTS.

Flavin-sensitized photoreduction of thymidine glycol

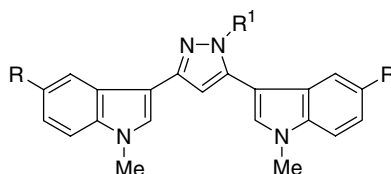
pp 6129–6133

Takeo Ito,* Akiko Kondo, Satoru Terada and Sei-ichi Nishimoto*

**3,5-Bis(3'-indolyl)pyrazoles, analogues of marine alkaloid nortopsentin: Synthesis and antitumor properties**

pp 6134–6137

Patrizia Diana,* Anna Carbone, Paola Barraja, Annamaria Martorana, Ornella Gia, Lisa DallaVia and Girolamo Cirrincione

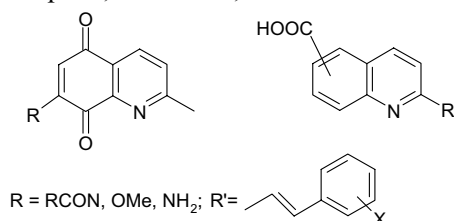


The synthesis and antitumor activity of novel 3,5-bis(3'-indolyl)pyrazole derivatives are reported.

**Investigating the antiproliferative activity of quinoline-5,8-diones and styrylquinolinecarboxylic acids on tumor cell lines**

pp 6138–6141

B. Podeszwa, H. Niedbala, J. Polanski,* R. Musiol, D. Tabak, J. Finster, K. Serafin, M. Milczarek, J. Wietrzyk, S. Boryczka, W. Mol, J. Jampilek, J. Dohnal, D. S. Kalinowski and D. R. Richardson

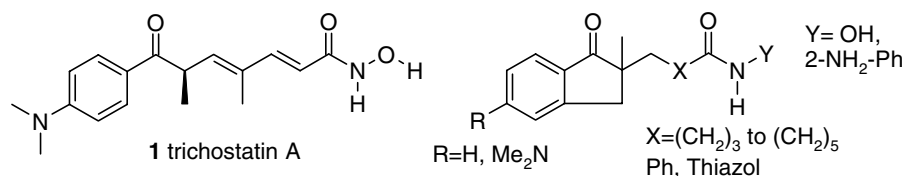


The structure–activity relationships of new quinoline-5,8-diones and quinolinecarboxylic acids exhibiting antiproliferative activity were investigated.

Antiproliferative activities of a library of hybrids between indanones and HDAC inhibitor SAHA and MS-275 analogues

pp 6142–6146

Cédric Charrier, Joëlle Roche, Jean-Pierre Gesson and Philippe Bertrand*



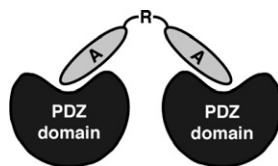
Hybrids of known histone deacetylases inhibitors (HDI) based on indanones were synthesized. Several alkylated indanones were obtained as hydroxamic acid and aminobenzamides derivatives and evaluated for their antiproliferative activity towards non small lung cancer cell line H661.



Bivalent peptides as PDZ domain ligands

pp 6147–6150

Edvin Klosi, Dorina Saro and Mark R. Spaller*



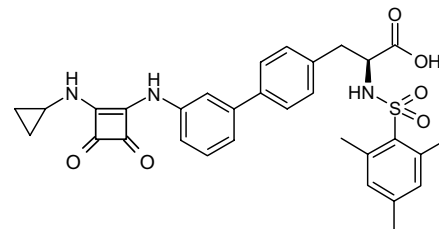
The design, synthesis, and thermodynamic binding evaluation of homobivalent peptides capable of binding two PDZ domain proteins is presented.

**Biphenyls as potent vitronectin receptor antagonists. Part 3: Squaric acid amides**

pp 6151–6154

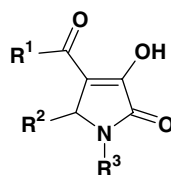
Klaus Urbahns,* Michael Härter, Markus Albers, Delf Schmidt, Beatrix Stelte-Ludwig, Ulf Brüggemeier, Andrea Vaupel, Jörg Keldenich, Klemens Lustig, Hideki Tsujishita and Christoph Gerdes

Vitronectin receptor ($\alpha_v\beta_3$) antagonists have been implicated as a possible new treatment of restenosis following balloon angioplasty. In this work we investigate a series of novel arginine mimetic scaffolds leading to new insight of the $\alpha_v\beta_3$ /ligand interaction. Squaric acid amide **10** is a subnanomolar $\alpha_v\beta_3$ antagonist with improved potency on human smooth muscle cell migration.

**10:** $\alpha_v\beta_3$: 0,5 nM; SMC: 10 nM**Substituted 2-pyrrolinone inhibitors of HIV-1 integrase**

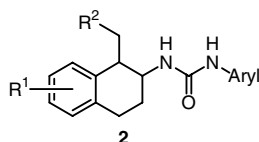
pp 6155–6159

Raveendra Dayam, Laith Q. Al-Mawsawi and Nouri Neamati*

**Heteroaryl β -tetralin ureas as novel antagonists of human TRPV1**

pp 6160–6163

Michele C. Jetter,* Mark A. Youngman, James J. McNally, Mark E. McDonnell, Sui-Po Zhang, Adrienne E. Dubin, Nadia Nasser, Ellen E. Codd, Christopher M. Flores and Scott L. Dax



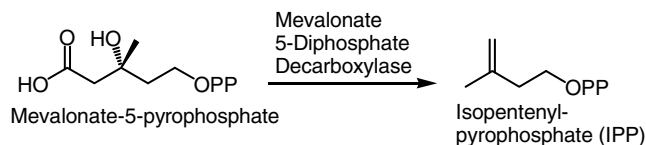
Aryl = 5-isoquinolinyl or 2-hydroxy-8-naphthyl

The synthesis and biological activity of a series of aminotetralin-derived heteroaryl urea TRPV1 antagonists is reported.

Mutation and inhibition studies of mevalonate 5-diphosphate decarboxylase

pp 6164–6168

Yongge Qiu, Jinbo Gao, Fei Guo, Yuqin Qiao and Ding Li*

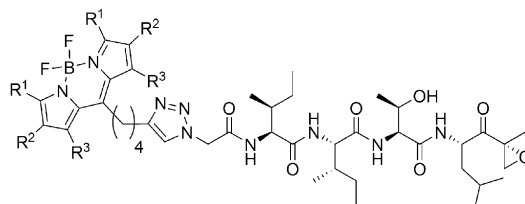


Mevalonate 5-diphosphate decarboxylase plays an important role in regulating cholesterol biosynthesis, which was studied through incubation with various synthetic substrate analogs and characterization of mutated enzymes.

Acetylene functionalized BODIPY dyes and their application in the synthesis of activity based proteasome probes

pp 6169–6171

Martijn Verdoes, Ulrik Hillaert, Bogdan I. Florea, Myra Sae-Heng, Martijn D. P. Risseuw, Dmitri V. Filippov, Gijsbert A. van der Marel and Herman S. Overkleeft*



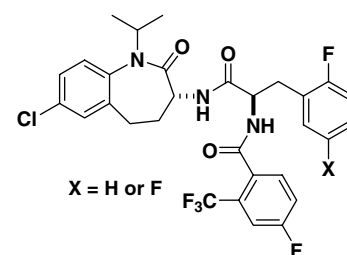
The synthesis of three acetylene functionalized BODIPY dyes is described. These dyes are used to synthesize a panel of fluorescent epoxomicin derived proteasome probes.

**Benzazepinone Na_v1.7 blockers: Potential treatments for neuropathic pain**

pp 6172–6177

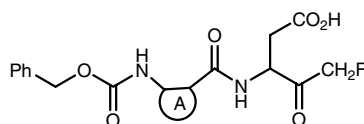
Scott B. Hoyt,* Clare London, Hyun Ok, Edward Gonzalez, Joseph L. Duffy, Catherine Abbadie, Brian Dean, John P. Felix, Maria L. Garcia, Nina Jochnowitz, Bindhu V. Karanam, Xiaohua Li, Kathryn A. Lyons, Erin McGowan, D. Euan MacIntyre, William J. Martin, Birgit T. Priest, McHardy M. Smith, Richard Tschirret-Guth, Vivien A. Warren, Brande S. Williams, Gregory J. Kaczorowski and William H. Parsons

A series of benzazepinones were synthesized and evaluated as hNa_v1.7 sodium channel blockers. Several compounds from this series displayed good oral bioavailability and exposure and were efficacious in a rat model of neuropathic pain.

**Dipeptidyl aspartyl fluoromethylketones as potent caspase inhibitors: Peptidomimetic replacement of the P₂ amino acid by 2-aminoaryl acids and other non-natural amino acids**

pp 6178–6182

Yan Wang, Shaojuan Jia, Ben Tseng, John Drewe and Sui Xiong Cai*



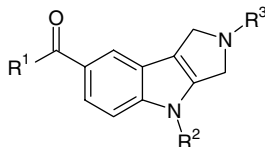
The synthesis and biological evaluation of a group of peptidomimetic 2-(Z-amino)benzamide-aspartyl fluoromethylketones and related compounds as caspase inhibitors are reported.



New 1,2,3,4-tetrahydropyrrolo[3,4-*b*]indole derivatives as selective CB2 receptor agonists

pp 6183–6187

Daniel Pagé,* Hua Yang, William Brown, Christopher Walpole, Manon Fleurent, Meredith Fyfe, François Gaudreault and Stéphane St-Onge

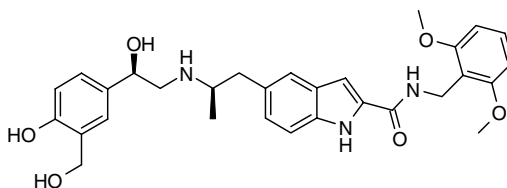


The preparation and evaluation of a novel class of CB2 agonists based on a 1,2,3,4-tetrahydropyrrolo[3,4-*b*]indole moiety are reported.

**The discovery of indole-derived long acting β_2 -adrenoceptor agonists for the treatment of asthma and COPD**

pp 6188–6191

Alan D. Brown, Mark E. Bunnage, Paul A. Glossop,* Mark Holbrook, Rhys D. Jones, Charlotte A. L. Lane, Russell A. Lewthwaite, Simon Mantell, Christelle Perros-Huguet, David A. Price* and Rob Webster

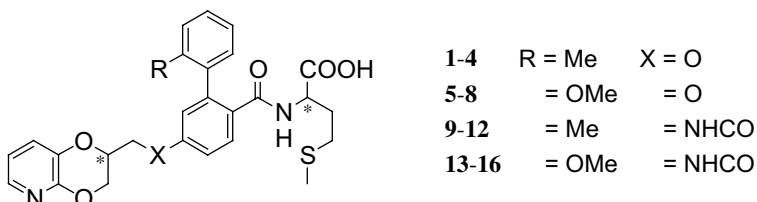


The design and profile of a series of indole containing long acting β_2 -adrenoceptor agonists is described. Evaluation of these analogues using an in vitro guinea pig trachea tissue model demonstrates that analogues within this series have salmeterol-like duration of action with potential for long duration of action in humans.

Peptidomimetic inhibitors of farnesyltransferase with high in vitro activity and significant cellular potency

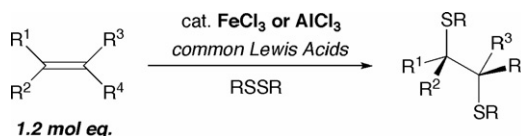
pp 6192–6196

Cristiano Bolchi, Marco Pallavicini, Chiara Rusconi, Luisa Diomede, Nicola Ferri, Alberto Corsini, Laura Fumagalli, Alessandro Pedretti, Giulio Vistoli and Ermanno Valoti*

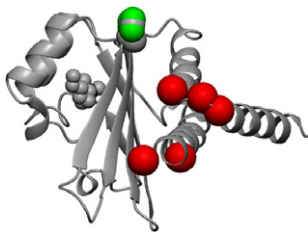
**Convenient method for the addition of disulfides to alkenes**

pp 6197–6201

Noriyuki Yamagiwa,* Yutaka Suto and Yasuhiro Torisawa*

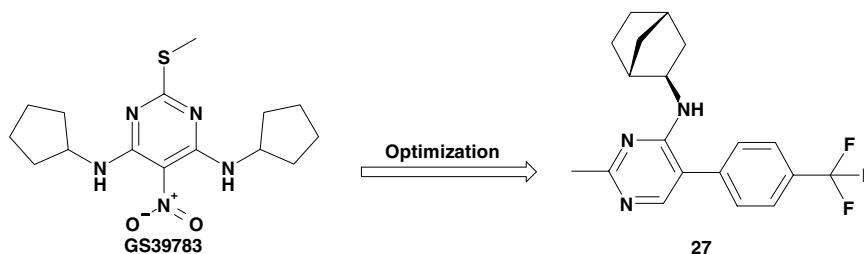


NMR detection of adventitious xylose binding to the quorum-sensing protein SdiA of *Escherichia coli* pp 6202–6205
Yong Yao, Tobin J. Dickerson,* Mark S. Hixon and H. Jane Dyson*

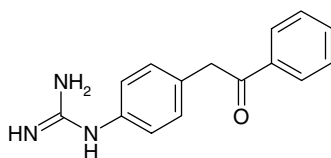


The anomalous ability of xylose to bind to the *Escherichia coli* quorum-sensing receptor protein SdiA is reported.

Syntheses and optimization of new GS39783 analogues as positive allosteric modulators of GABA_B receptors pp 6206–6211
Sébastien Guery,* Philipp Floersheim, Klemens Kaupmann* and Wolfgang Froestl*



Geometry of GPPE binding to picrate and to the urokinase type plasminogen activator pp 6212–6214
Ewa Źesławska, Jörg Stürzebecher and Barbara J. Oleksyn*

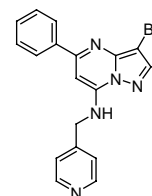


We have investigated the conformation of a uPA inhibitor in different crystalline environments. The crystal structures of the urokinase-type plasminogen activator in complex with GPPE and GPPE-picrate were determined.



Versatile templates for the development of novel kinase inhibitors: Discovery of novel CDK inhibitors pp 6216–6219
Michael P. Dwyer,* Kamil Paruch,* Carmen Alvarez, Ronald J. Doll, Kerry Keertikar, Jose Duca, Thierry O. Fischmann, Alan Hruza, Vincent Madison, Emma Lees, David Parry, Wolfgang Seghezzi, Nicole Sgambellone, Frances Shanahan, Derek Wiswell and Timothy J. Guzi

Pyrazolo[1,5-*a*]pyrimidine **9** emerged as a key template for further optimization toward the identification of CDK inhibitors.



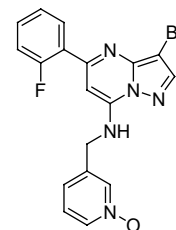
9 CDK2 IC₅₀ = 0.029 uM

Pyrazolo[1,5-*a*]pyrimidines as orally available inhibitors of cyclin-dependent kinase 2

pp 6220–6223

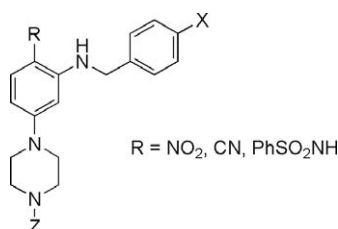
Kamil Paruch,* Michael P. Dwyer,* Carmen Alvarez, Courtney Brown, Tin-Yau Chan, Ronald J. Doll, Kerry Keertikar, Chad Knutson, Brian McKittrick, Jocelyn Rivera, Randall Rossman, Greg Tucker, Thierry O. Fischmann, Alan Hruza, Vincent Madison, Amin A. Nomeir, Yaolin Wang, Emma Lees, David Parry, Nicole Sgambellone, Wolfgang Seghezzi, Lesley Schultz, Fran Shanahan, Derek Wiswell, Xiaoying Xu, Quiao Zhou, Ray A. James, Vidyadhar M. Paradkar, Haengsoon Park, Laura R. Rokosz, Tara M. Stauffer and Timothy J. Guzi

Properly substituted pyrazolo[1,5-*a*]pyrimidines are potent and selective CDK2 inhibitors. Compound **15j** is orally available and showed efficacy in mouse A2780 xenograft model.

**15j** CDK2 IC₅₀ = 0.013 μM**Discovery of 5-HT₆ receptor ligands based on virtual HTS**

pp 6224–6229

Stefan Tasler,* Jürgen Kraus, Andreas Wuzik, Oliver Müller, Andrea Aschenbrenner, Elena Cubero,* Rosalia Pascual, Jordi-Ramon Quintana-Ruiz, Alberto Dordal, Ramon Mercè and Xavier Codony

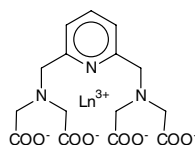


The discovery and SAR studies of 5-HT₆ ligands are described.

In vitro characterization of the Gd complex of [2,6-pyridinediylbis(methylene nitrilo)] tetraacetic acid (PMN-tetraacetic acid) and of its Eu analogue, suitable bimodal contrast agents for MRI and optical imaging

pp 6230–6233

S. Laurent,* L. Vander Elst, M. Wautier, C. Galaup, R. N. Muller and C. Picard

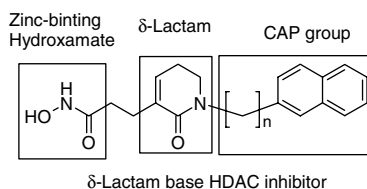


Gd and Eu complexes of PMN-tetraacetic acid show interesting properties for MRI and optical imaging.

Modification of cap group in δ-lactam-based histone deacetylase (HDAC) inhibitors

pp 6234–6238

Hwan Mook Kim, Sung Hee Hong, Myung Sook Kim, Chang Woo Lee, Jong Soon Kang, Kiho Lee, Song-Kyu Park, Jeung Whan Han, Hee Yoon Lee, Yongseok Choi, Ho Jeung Kwon and Gyoonee Han*

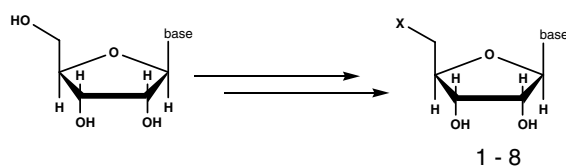


Novel δ-lactam-based HDAC inhibitors with various substituted benzyl or bi-aromatic CAP groups were prepared using ring closure metathesis reaction, and their HDAC inhibitory activities and anti-proliferative effects evaluated.

Synthesis and antimicrobial activity of some novel nucleoside analogues of adenosine and 1,3-dideazaadenosine

pp 6239–6244

Richa Srivastava, Anudita Bhargava and Ramendra K. Singh*



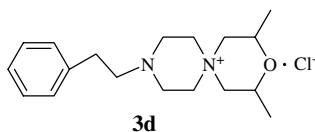
Compound	Base	X
1	adenine	-SCH ₂ CH ₂ COOH
2	adenine	-SCH ₂ CH ₂ CONH ₂
3	adenine	-SCH ₂ CH ₂ COOC ₂ H ₅
4	1,3-dideazaadenine	-SCH ₂ CH ₂ COOH
5	1,3-dideazaadenine	-SCH ₂ CH ₂ CONH ₂
6	1,3-dideazaadenine	-SCH ₂ CH ₂ COOC ₂ H ₅
7	6-nitro-1,3-dideazaadenine	-SCH ₂ -CH=CH ₂
8	6-nitro-8-ethyl-1,3-dideazaadenine	-SCH ₂ -CH=CH ₂

All the newly synthesized compounds are structurally analogous to SAH molecule and have shown good antifungal and antibacterial activity.

Unique spirocyclopiperazinium salt III: Further investigation of monospirocyclopiperazinium (MSPZ) salts as potential analgesics

pp 6245–6249

Qi Sun, Cai-Qin Yue, Jia Ye, Chang-Ling Li, Tie-Ming Cheng and Run-Tao Li*

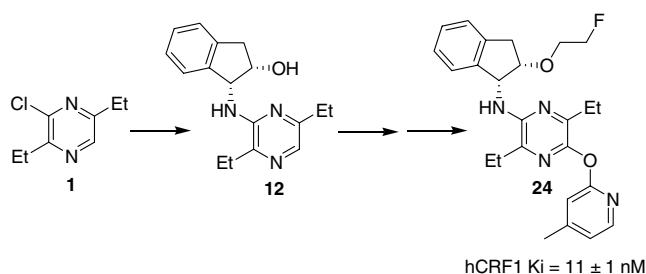


65% inhibition in acetic acid writhing
test at dose of 31 μ mol/kg;
LD₅₀ = 1.55 mmol/kg, ip.

**Heteroatom-linked indanylpyrazines are corticotropin releasing factor type-1 receptor antagonists**

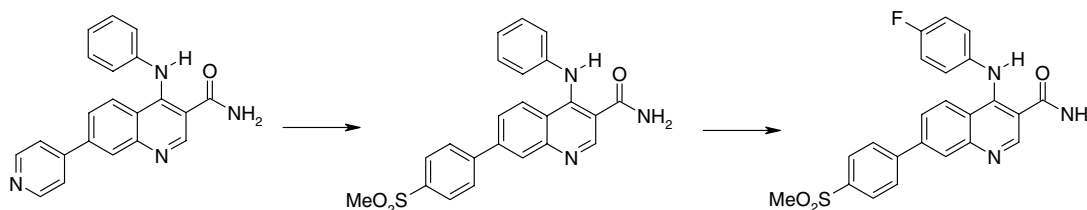
pp 6250–6256

Jeffrey W. Corbett,* Mark R. Rauckhorst, Fang Qian, Robert L. Hoffman, Christopher S. Knauer and Lawrence W. Fitzgerald

**Synthesis of novel anilinoquinolines as *c-fms* inhibitors**

pp 6257–6260

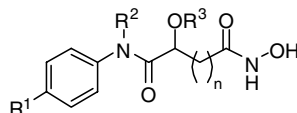
Terrence L. Smalley, Jr.,* Stanley D. Chamberlain, Wendy Y. Mills, David L. Musso, Sab A. Randhawa, John A. Ray, Vicente Samano and Lloyd Frick



ω -Alkoxy analogues of SAHA (vorinostat) as inhibitors of HDAC: A study of chain-length and stereochemical dependence

pp 6261–6265

Stephen Hanessian,* Luciana Auzzas, Giuseppe Giannini, Mauro Marzi, Walter Cabri, Marcella Barbarino, Loredana Vesci and Claudio Pisano

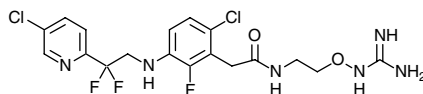


The synthesis of a series of ω -alkoxy ethers analogues of suberoylanilide hydroxamic acid, and their HDAC inhibitory and antiproliferative activity on human cell lines are reported.

**2-(2-Chloro-6-fluorophenyl)acetamides as potent thrombin inhibitors**

pp 6266–6269

Lily Lee, Kevin D. Kreutter, Wenxi Pan, Carl Crysler, John Spurlino, Mark R. Player,* Bruce Tomczuk and Tianbao Lu



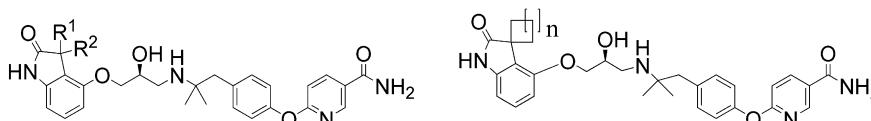
K_i (thrombin) = 1.8 nM

2-(2-Chloro-6-fluorophenyl)acetamides having 2,2-difluoro-2-aryl/heteroaryl-ethylamine P3 and oxyguanidine P1 substituents are potent thrombin inhibitors (K_i = 0.9–33.9 nM). 2-(5-Chloro-pyridin-2-yl)-2,2-difluoroethylamine was the best P3 substituent, yielding the most potent inhibitor (K_i = 0.7 nM). Replacing the P3 heteroaryl group with a phenyl ring or replacing the difluoro substitution with dimethyl or cyclopropyl groups in the linker reduced the affinity for thrombin significantly. The aminopyridine P1s also provided an increase in potency.

Potent oxindole based human β_3 adrenergic receptor agonists

pp 6270–6273

F. Craig Stevens, William E. Bloomquist, Anthony G. Borel, Marlene L. Cohen, Christine A. Droste, Mark L. Heiman, Aidas Kriauciunas, Daniel J. Sall, Frank C. Tinsley and Cynthia D. Jesudason*



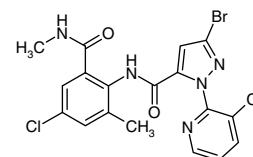
The synthesis and biological evaluation of a series of oxindole β_3 adrenergic receptor agonists is described. A modulation of rat atrial tachycardia was observed with substitution at the 3-position of the oxindole moiety.

Rynaxypyr™: A new insecticidal anthranilic diamide that acts as a potent and selective ryanodine receptor activator

pp 6274–6279

George P. Lahm,* Thomas M. Stevenson, Thomas P. Selby, John H. Freudenberger, Daniel Cordova, Lindsey Flexner, Cheryl A. Bellin, Christine M. Dubas, Ben K. Smith, Kenneth A. Hughes, J. Gary Hollingshaus, Christopher E. Clark and Eric A. Benner

This paper describes the discovery of Rynaxypyr™, the first member from a novel class of anthranilic diamides, with exceptional activity against insects of the order Lepidoptera. Rynaxypyr™ has been found to exhibit its action by release of intracellular Ca^{2+} stores mediated by the ryanodine receptor. A comparison of *Heliothis virescens* (*Hv*) ryanodine receptor activity is made versus insecticidal potency on a series of Lepidoptera, including *Hv*. Remarkably high differential receptor selectivity is also demonstrated between insect and mammalian cell lines in support of the low mammalian toxicity.

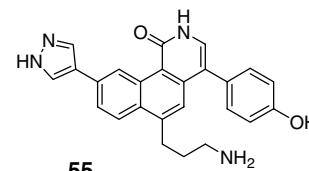


Synthesis and evaluation of substituted benzoisoquinolinones as potent inhibitors of Chk1 kinase

pp 6280–6285

Robert M. Garbaccio,* Shaei Huang, Edward S. Tasber, Mark E. Fraley, Youwei Yan, Sanjeev Munshi, Mari Ikuta, Lawrence Kuo, Constanine Kreatsoulas, Steve Stirdivant, Bob Drakas, Keith Rickert, Eileen S. Walsh, Kelly A. Hamilton, Carolyn A. Buser, James Hardwick, Xianzhi Mao, Stephen C. Beck, Marc T. Abrams, Weikang Tao, Rob Lobell, Laura Sepp-Lorenzino and George D. Hartman

Benzoisoquinolinones (i.e., **55**) are reported as potent inhibitors of Chk1 kinase.

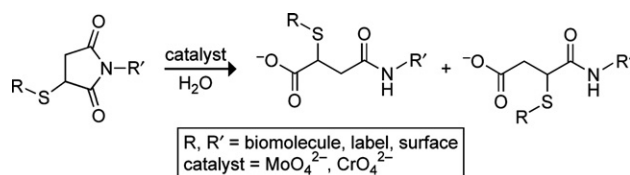
**55**

Chk1 IC₅₀ = 0.3 nM
Cell EC₅₀ = 47 nM

**Catalysis of imido group hydrolysis in a maleimide conjugate**

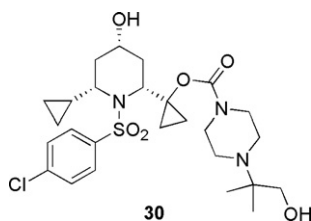
pp 6286–6289

Jeet Kalia and Ronald T. Raines*

**Discovery of 2,4,6-trisubstituted *N*-arylsulfonyl piperidines as γ -secretase inhibitors**

pp 6290–6294

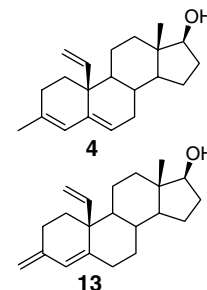
Hongmei Li,* Theodoros Asberom, Thomas A. Bara, John W. Clader, William J. Greenlee, Hubert B. Josien, Mark D. McBriar, Amin Nomeir, Dmitri A. Pissarnitski, Murali Rajagopalan, Ruo Xu, Zhiqiang Zhao, Lixin Song and Lili Zhang

**30****Androstene-3,5-dienes as ER- β selective SERMs**

pp 6295–6298

Timothy A. Blizzard,* Candido Gude, Jerry D. Morgan, Wanda Chan, Elizabeth T. Birzin, Marina Mojena, Consuelo Tudela, Fang Chen, Kristin Knecht, Qin Su, Bryan Kraker, Ralph T. Mosley, Mark A. Holmes, Susan P. Rohrer and Milton L. Hammond

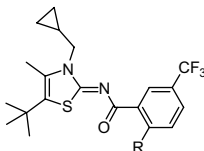
A series of androstene-3,5-dienes (e.g., **4** and **13**) is reported. Compound **4** exhibits excellent binding affinity and selectivity for ER- β over ER- α and AR and is a potent ER- β agonist despite lacking the traditional hydroxyl substitution at C-3.

**13**

N-Alkylidenearylcarboxamides as new potent and selective CB₂ cannabinoid receptor agonists with good oral bioavailability

pp 6299–6304

Hiroshi Ohta,* Tomoko Ishizaka, Makoto Tatsuzuki, Mitsukane Yoshinaga, Izumi Iida, Yasumitsu Tomishima, Yoshihisa Toda and Shuji Saito



R = H : **4-9** CB₂ IC₅₀ = 13 nM *F* = 52%
 R = OMe : **4-27** CB₂ IC₅₀ = 1.2 nM

Compounds **4-9** and **4-27** had high affinities for the human CB₂ receptor (CB₂ IC₅₀ = 13 nM and 1.2 nM) and a high selectivity for CB₂ (CB₁ IC₅₀/CB₂ IC₅₀ = 270 and 1600). Furthermore, compound **4-9** had good oral bioavailability (*F* = 52%, 3 mg/kg).



Synthesis of (aryloxyacetyl amino)-isonicotinic/nicotinic acid analogues as potent hypoxia-inducible factor (HIF)-1α inhibitors

pp 6305–6310

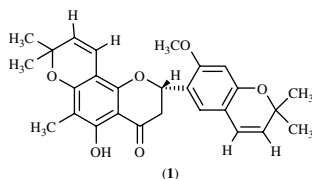
Shanthaveerappa K. Boovanahalli, Xuejun Jin, Yinglan Jin, Jin Hwan Kim, Nguyen Tien Dat, Young-Soo Hong, Jeong Hyung Lee, Sang-Hun Jung, Kyeong Lee* and Jung Joon Lee*



A novel flavonoid from *Lespedeza virgata* (Thunb.) DC.: Structural elucidation and antioxidative activity

pp 6311–6315

Li Tan, Xiu-Feng Zhang, Bao-Zhen Yan, Hai-Ming Shi, Li-Bo Du, Ya-Zhou Zhang, Lan-Fen Wang, Ya-Lin Tang and Yang Liu*

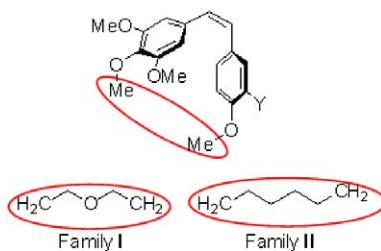


From *Lespedeza virgata* (Thunb.) DC. five known and one new (1) flavonoids were isolated. This new compound when tested in superoxide anion scavenging assay exerted the highest antioxidant activity (IC₅₀ = 0.14 mg/ml).

Conformationally restricted macrocyclic analogues of combretastatins

pp 6316–6320

Carmen Mateo, Raquel Álvarez, Concepción Pérez-Melero, Rafael Peláez* and Manuel Medarde*

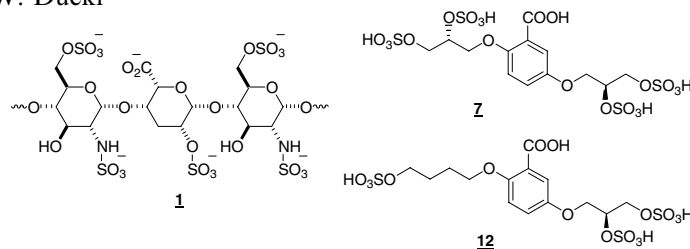


The activity as inhibitors of tubulin polymerization of macrocyclic analogues of combretastatins is reported.

Novel heparin/heparan sulfate mimics as inhibitors of HGF/SF-induced MET activation

pp 6321–6325

Eun-Ang Raiber, James A. Wilkinson,* Fabrizio Manetti, Maurizio Botta, Jon Deakin, John Gallagher, Malcolm Lyon and Sylvie W. Ducki*



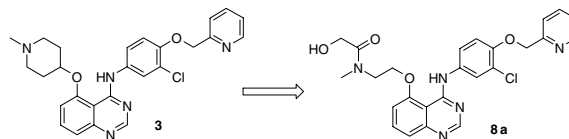
The synthesis of simple, non-sugar glycosaminoglycan (GAG) mimics has been achieved and the analogues evaluated for their ability to inhibit the activation of the MET receptor by hepatocyte growth factor/scatter factor (HGF/SF).

Neutral 5-substituted 4-anilinoquinazolines as potent, orally active inhibitors of erbB2 receptor tyrosine kinase

pp 6326–6329

Peter Ballard, Bernard C. Barlaam, Robert H. Bradbury,* Allan Dishington, Laurent F. A. Hennequin, D. Mark Dickinson, Ian M. Hollingsworth, Jason G. Kettle, Teresa Klinowska, Donald J. Ogilvie, Stuart E. Pearson, James S. Scott, Abid Suleman, Robin Whittaker, Emma J. Williams, Robin Wood and Lindsay Wright

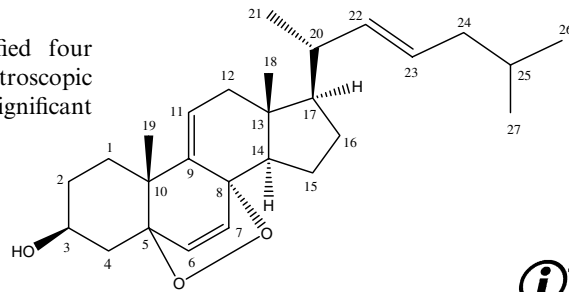
Neutral 5-substituted 4-anilinoquinazolines addressed high in vivo clearance and phospholipidosis associated with previous basic compounds such as 3, and a representative compound 8a inhibited tumor growth in a mouse xenograft model when co-administered with the cytochrome P450 inhibitor 1-aminobenzotriazole (ABT).

**New biologically active epidioxysterols from *Stereum hirsutum***

pp 6330–6334

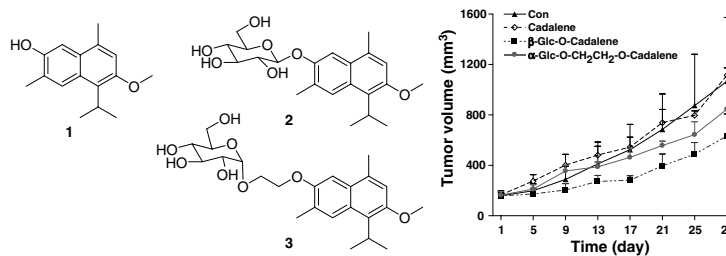
Francesca Cateni,* Bojan Doljak, Marina Zacchigna, Marko Anderluh, Andrej Piltaver, Giuditta Scialino and Elena Banfi

From the fungus *Stereum hirsutum* have been isolated and identified four epidioxysterols. Their structures were elucidated on the basis of spectroscopic analysis and chemical reactions. Epidioxysterols were found to show significant activity against *Mycobacterium tuberculosis*.

**Enhanced efficacy of 7-hydroxy-3-methoxycadaleone via glycosylation in in vivo xenograft study**

pp 6335–6339

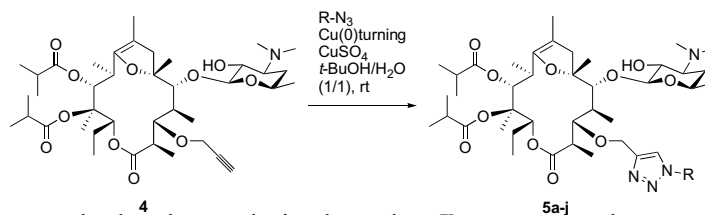
Hyang Yeon Lee, Jung-Taek Kwon, Minseob Koh, Myung-Haing Cho* and Seung Bum Park*



Design and synthesis via click chemistry of 8,9-anhydroerythromycin A 6,9-hemiketal analogues with anti-MRSA and -VRE activity

pp 6340–6344

Akihiro Sugawara, Toshiaki Sunazuka, Tomoyasu Hirose, Kenichiro Nagai, Yukie Yamaguchi, Hideaki Hanaki, K. Barry Sharpless and Satoshi Ōmura*



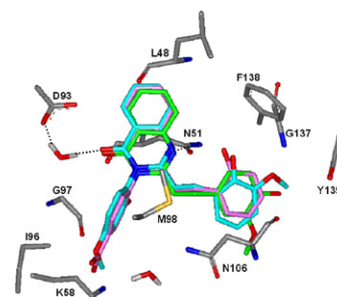
One of 10 kinds of triazole compounds, the adamantyl-triazole product **5b**, was produced as a potential lead of new antibiotic for use against MRSA and VRE strains, using click methodology.

A novel class of Hsp90 inhibitors isolated by structure-based virtual screening

pp 6345–6349

Hwangseo Park, Yun-Jung Kim and Ji-Sook Hahn*

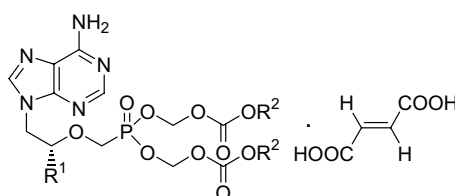
A novel class of 3-phenyl-2-styryl-3H-quinazolin-4-one Hsp90 inhibitors with in vitro anti-tumor activity is identified by structure-based virtual screening of a chemical database with docking simulations in the N-terminal ATP-binding site, in vitro ATPase assay using yeast Hsp90, and cell-based Her2 degradation assay in a consecutive fashion.



Some new acyclic nucleotide analogues as antiviral prodrugs: Synthesis and bioactivities in vitro

pp 6350–6353

Yan-bo Tang, Zong-gen Peng, Zong-ying Liu, Yan-ping Li, Jian-dong Jiang and Zhuo-rong Li*



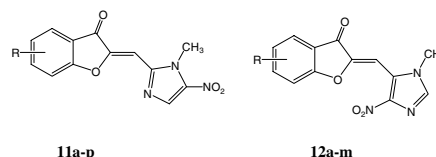
A series of new acyclic nucleotide analogues were synthesized and tested for in vitro antiviral activity against HIV/HBV. Most of tested compounds exhibited potent antiviral activity.

Synthesis, antibacterial activity, and quantitative structure–activity relationships of new (Z)-2-(nitroimidazolymethylene)-3(2H)-benzofuranone derivatives

pp 6354–6363

Narges Hadj-esfandiari, Latifeh Navidpour, Hooman Shadnia, Mohsen Amini, Nasrin Samadi, Mohammad Ali Faramarzi and Abbas Shafiee*

Synthesis, biological evaluation, and QSAR analysis of a novel class of (Z)-2-(nitroimidazolymethylene)-3(2H)-benzofuranone derivatives (**11a–p** and **12a–m**) as antibacterial agents are described.

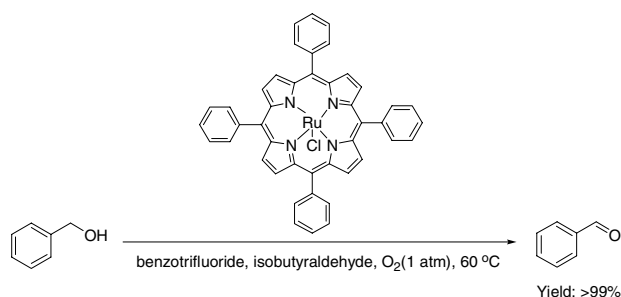


R = H, 5-Cl, 5-Me, 5-OMe, 5-Br, 5-I, 5-NO₂, 6-Cl, 6-Me, 6-OMe, 7-Cl, 7-Me, 7-OMe, 6,7-(OMe)₂, 6-OH, 4,6-(OH)₂

Highly efficient selective oxidation of alcohols to carbonyl compounds catalyzed by ruthenium (III) *meso*-tetraphenylporphyrin chloride in the presence of molecular oxygen

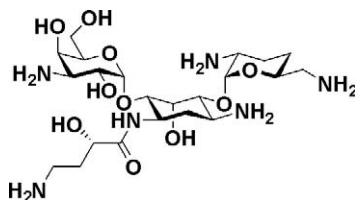
pp 6364–6368

Hong-Bing Ji,* Qiu-Lan Yuan, Xian-Tai Zhou, Li-Xia Pei and Le-Fu Wang

**Effect of varying the 4''-position of arbekacin derivatives on antibacterial activity against MRSA and *Pseudomonas aeruginosa***

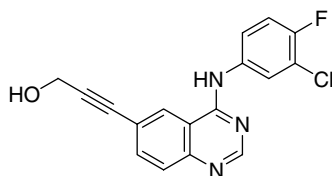
pp 6369–6372

Yukiko Hiraiwa, Nobuto Minowa,* Takayuki Usui,* Yoshihisa Akiyama, Kazunori Maebashi and Daishiro Ikeda*

**Synthesis and biological evaluation of substituted 6-alkynyl-4-anilinoquinazoline derivatives as potent EGFR inhibitors**

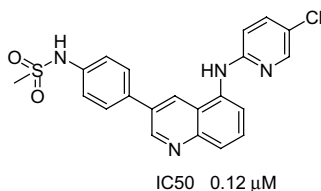
pp 6373–6377

Lee Tai Liu,* Ta-Tung Yuan, Hung-Huang Liu, Shyh-Fong Chen and Ying-Ta Wu

IC₅₀ 14 nM for in vitro EGFR kinase inhibition.**3,5-Disubstituted quinolines as novel c-Jun N-terminal kinase inhibitors**

pp 6378–6382

Rong Jiang,* Derek Duckett, Weiming Chen, Jeff Habel, Yuan Yuan Ling, Philip LoGrasso and Theodore M. Kamenecka



A novel series of c-Jun N-terminal kinase (JNK) inhibitors based on 3,5-disubstituted quinolines are reported.

Effects of quinones on free-radical processes of oxidation and fragmentation of hydroxyl-containing organic compounds

pp 6383–6386

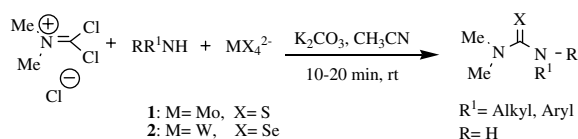
O. I. Shadyro,* A. A. Sosnovskaya, I. P. Edimecheva, N. I. Ostrovskaya,
K. M. Kazem, I. B. Hryntsevich and A. V. Alekseev

The effects of coenzymes Q, Vitamin K₃ and synthetic quinones on free-radical processes of oxidation and fragmentation of hydroxyl-containing organic compounds have been studied.

Facile one-pot synthesis of thio and selenourea derivatives: A new class of potent urease inhibitors

pp 6387–6391

Kirubakaran Sivapriya, Perumal Suguna, Arun Banerjee, Vadivelu Saravanan,
Desirazu N. Rao and Srinivasan Chandrasekaran*

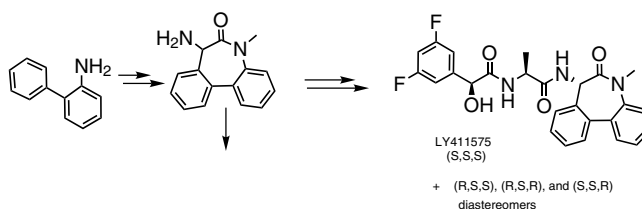


A facile, one-pot synthesis of thio and selenourea derivatives is reported. Some of the derivatives showed potent inhibitory activity against urease (jack bean) in the nanomolar range.

A multigram chemical synthesis of the γ -secretase inhibitor LY411575 and its diastereoisomers

pp 6392–6395

Abdul H. Fauq,* Katherine Simpson, Ghulam M. Maharvi, Todd Golde and Pritam Das


OTHER CONTENTS

Summary of instructions to authors

p I

*Corresponding author

* Supplementary data available via ScienceDirect

COVER

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

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