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Bioorganic & Medicinal Chemistry Letters

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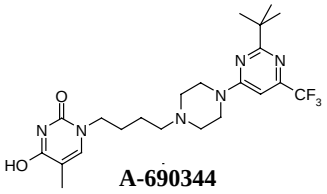
# Contents

## ARTICLES

**Synthesis and SAR of highly potent and selective dopamine $D_3$-receptor antagonists: 1*H*-Pyrimidin-2-one derivatives** **pp 490–494**

Hervé Geneste,* Gisela Backfisch, Wilfried Braje, Jürgen Delzer, Andreas Haupt, Charles W. Hutchins, Linda L. King, Andreas Kling, Hans-Jürgen Teschendorf, Liliane Unger and Wolfgang Wernet

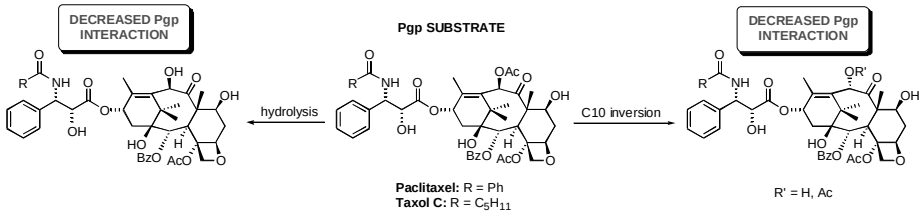


**A-690344**

The synthesis and SAR of novel highly potent and selective dopamine $D_3$-receptor antagonists based on a 1*H*-pyrimidin-2-one scaffold are described. **A-690344** antagonized PD 128907-induced huddling deficits in rat ($ED_{50}$ 6.1mg/kg po), a social interaction paradigm.

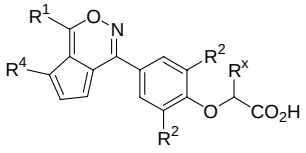
**Single-site chemical modification at C10 of the baccatin III core of paclitaxel and Taxol C reduces P-glycoprotein interactions in bovine brain microvessel endothelial cells** **pp 495–498**

Jared T. Spletstoser, Brandon J. Turunen, Kelly Desino, Antonie Rice, Apurba Datta, Dinah Dutta, Jacquelyn K. Huff, Richard H. Himes,* Kenneth L. Audus,* Anna Seelig* and Gunda I. Georg*

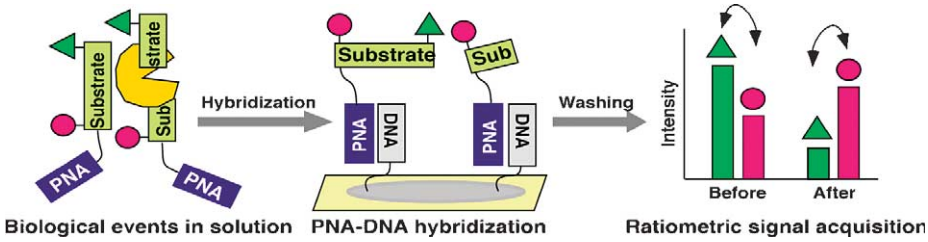



**PTP-1B inhibitors: Cyclopenta[*d*][1,2]-oxazine derivatives** **pp 499–502**

Sung Yun Cho, Ji Yoen Baek, Sang Sub Han, Seung Kyu Kang, Jae Du Ha, Jin Hee Ahn, Jae Don Lee, Kwang Rok Kim, Hyae Gyeong Cheon, Sang Dal Rhee, Sung Don Yang, Gyu Hwan Yon, Chwang Siek Pak and Joong-Kwon Choi*



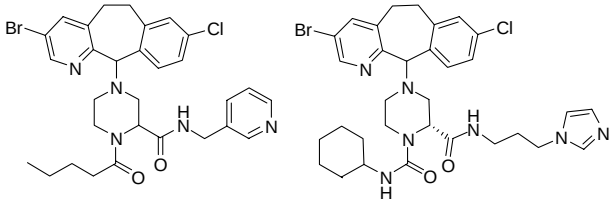
**A PNA–DNA hybridization chip approach for the detection of β-secretase activity** **pp 503–506**
Shusuke Sano, Kin-ya Tomizaki, Kenji Usui and Hisakazu Mihara*




The PNA–DNA complementary hybridization chip technology utilizing a PNA-encoded peptide substrate allowed us to detect β-secretase activity 10 times more sensitively than assays in solution.

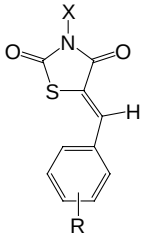
**Guiding farnesyltransferase inhibitors from an ECLiPS® library to the catalytic zinc** **pp 507–511**
Chia-Yu Huang, Tara M. Stauffer, Corey L. Strickland, John C. Reader, He Huang, Ge Li, Alan B. Cooper, Ronald J. Doll, Ashit K. Ganguly, John J. Baldwin and Laura L. Rokosz*

Compounds **8** and **41** are potent analogs of farnesyltransferase inhibitors that were identified from an ECLiPS® library screen. X-ray crystallographic analyses of inhibited complexes show that the side-chain pyridyl of **8** and the imidazoyl of **41** coordinate to the active site zinc.

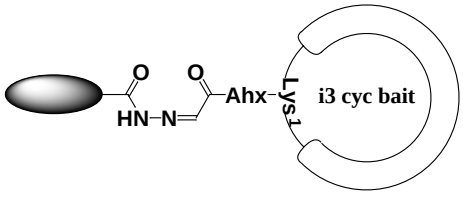



**Quantitative structure–activity analysis of 5-arylidene-2,4-thiazolidinediones as aldose reductase inhibitors** **pp 512–520**
S. V. Sambasivarao, Love K. Soni,* Arun K. Gupta, P. Hanumantharao and S. G. Kaskhedikar

3D-QSAR analysis, Hansch analysis, and Fujita-Ban analysis were performed on a series of 5-arylidene-2,4-thiazolidinediones as aldose reductase inhibitors. The 2D & 3D-QSAR models were generated using 18 compounds and Fujita-Ban analysis models were obtained using 23 compounds. The predictive ability of the resulting 2D and 3D models was evaluated against a test set of 5 compounds. Analyses of results from the present QSAR study inferred that 3rd position of the phenyl ring and acetic acid substitution at *N*-position of thiazolidinediones play a key role in the aldose reductase inhibitory activity.

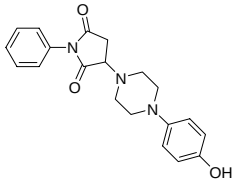



**Design and synthesis of cyclic and linear peptide-agarose tools for baiting interacting protein partners of GPCRs** **pp 521–524**
Sébastien Granier, Frédéric Jean-Alphonse, Hélène Déméné, Gilles Guillon, Robert Pascal* and Christiane Mendre*



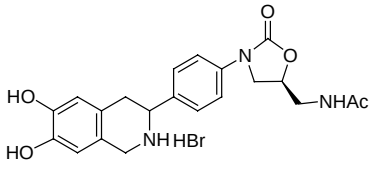

The synthesis of affinity supports designed to identify GPCR partners is reported.

**In silico design and synthesis of piperazine-1-pyrrolidine-2,5-dione scaffold-based novel malic enzyme inhibitors** pp 525–528
Y. John Zhang,* Zhaolin Wang, Dennis Sprous and Roustem Nabioullin



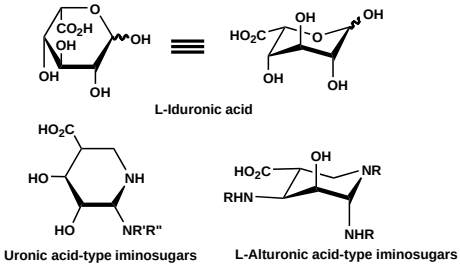
Fragment-based virtual library design and virtual screening have been conducted against malic enzyme (ME) homology model. Compounds from this library have shown submicromolar inhibitory activity against malic enzyme.

**New potential antibacterials: A synthetic route to *N*-aryloxazolidinone/3-aryltetrahydroisoquinoline hybrids** pp 529–531
Rosa Griera, Carme Cantos-Llopart, Mercedes Amat, Joan Bosch,* Juan-C. del Castillo and Joan Huguet



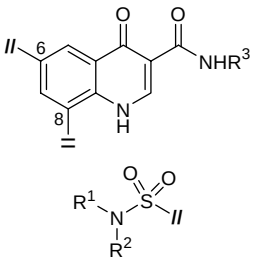
**Synthesis and biological evaluation of *gem*-diamine 1-*N*-iminosugars related to L-iduronic acid as inhibitors of heparan sulfate 2-*O*-sulfotransferase** pp 532–536
Jillian R. Brown, Yoshio Nishimura and Jeffrey D. Esko*

A variety of *gem*-diamine 1-*N*-iminosugars related to L-iduronic acid were synthesized and evaluated as inhibitors of heparan sulfate uronyl 2-*O*-sulfotransferase using an in vitro enzyme assay. Two iminosugars containing guanidino groups acted as potent in vitro inhibitors of the enzyme.

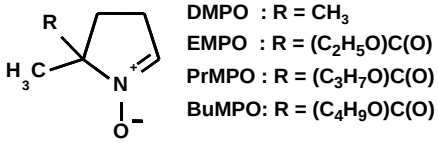



**Sulfamoyl-4-oxoquinoline-3-carboxamides: Novel potentiators of defective ΔF508-cystic fibrosis transmembrane conductance regulator chloride channel gating** pp 537–540
Yat Fan Suen, Lori Robins, Baoxue Yang, A. S. Verkman, Michael H. Nantz and Mark J. Kurth*

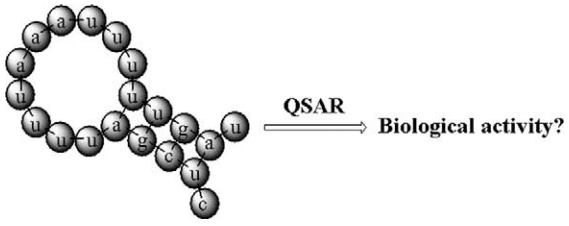
Evaluation and synthesis of sulfamoyl-4-oxoquinoline-3-carboxamide correctors of defective gating of the ΔF508-cystic fibrosis transmembrane conductance regulator chloride channel are reported.



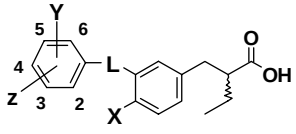
**Cytotoxicity of novel derivatives of the spin trap EMPO** **pp 541–546**
Nataliya Rohr-Udilova, Klaus Stolze, Brigitte Marian and Hans Nohl*




**QSAR study for mycobacterial promoters with low sequence homology** **pp 547–553**
Humberto González-Díaz,* Alcides Pérez-Bello, Eugenio Uriarte and Yenny González-Díaz

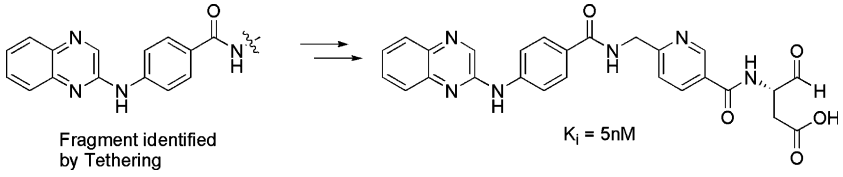



**Design and synthesis of substituted phenylpropanoic acid derivatives as human peroxisome proliferator-activated receptor α/δ dual agonists** **pp 554–558**
Jun-ichi Kasuga, Makoto Makishima, Yuichi Hashimoto and Hiroyuki Miyachi*

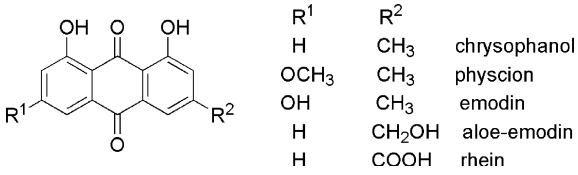



The PPAR agonist with dual PPARα/δ activity is reported.

**Tethering identifies fragment that yields potent inhibitors of human caspase-1** **pp 559–562**
Bruce T. Fahr,* Tom O'Brien, Phuongly Pham, Nathan D. Waal, Subramanian Baskaran, Brian C. Raimundo, Joni W. Lam, Michelle M. Sopko, Hans E. Purkey and Michael J. Romanowski

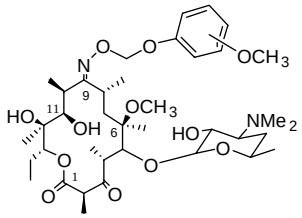


**Isolation and inhibitory activity against ERK Phosphorylation of hydroxyanthraquinones from rhubarb** **pp 563–568**
Xia Zhou, Baoan Song,* Linhong Jin, Deyu Hu, Chunling Diao, Guangfang Xu, Zhihui Zou and Song Yang




The extraction and isolation of five hydroxyanthraquinones, chrysophanol, physcion, emodin, aloe-emodin, and rhein from Chinese medicinal herb rhubarb, is developed. And their inhibitory activity against ERK phosphorylation and antifungal activity are performed.

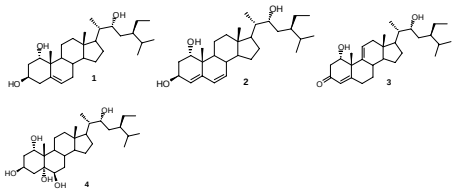
**Design, synthesis, and anti-*Helicobacter pylori* activity of erythromycin A (*E*)-9-oxime ether derivatives** **pp 569–572**
Ghilsoo Nam, Tae Won Kang, Jung Hyu Shin and Kyung Il Choi*




**II**

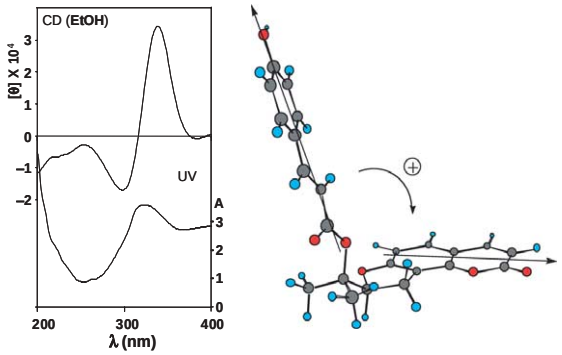
Oxime ether formation at C-9 carbonyl and methylation at C-6 hydroxy group of erythromycin A followed by transformation to ketolides gave the derivative II, which exhibited comparable in vitro anti-*H. pylori* activity and improved acid stability compared to the reference compound clarithromycin.

**Isolation and cholinesterase-inhibition studies of sterols from *Haloxylon recurvum*** **pp 573–580**
Ejaz Ahmed, Sarfraz A. Nawaz, Abdul Malik* and M. Iqbal Choudhary

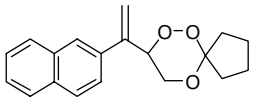



Haloxysterols A–D (**1**–**4**), together with 5 known sterols (**5**–**9**), were isolated from the whole plant of *Haloxylon recurvum*. The structures were elucidated on the basis of spectral methods, especially 2D-NMR spectra (HMQC, HMBC, and NOESY). All the compounds showed potent inhibitory activity against cholinesterase enzyme.

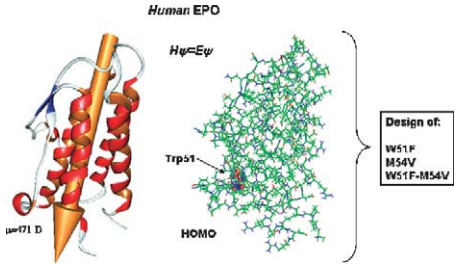
**Angelmarin, a novel anti-cancer agent able to eliminate the tolerance of cancer cells to nutrient starvation** **pp 581–583**
Suresh Awale, Eduardo M. N. Nakashima, Surya K. Kalauni, Yasuhiro Tezuka, Yukiko Kurashima, Jie Lu, Hiroyasu Esumi and Shigetoshi Kadota*



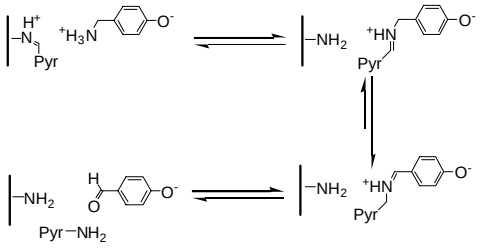
**8-(1-Naphthalen-2-yl-vinyl)-6,7,10-trioxaspiro (4.5) decane, a new 1,2,4-trioxane effective against rodent and simian malaria** **pp 584–586**
Chandan Singh,* Rani Kanchan, Divya Srivastava and Sunil K. Puri



**The electronic structure of human erythropoietin as an aid in the design of oxidation-resistant therapeutic proteins** **pp 587–591**
Fabio Pichierri*

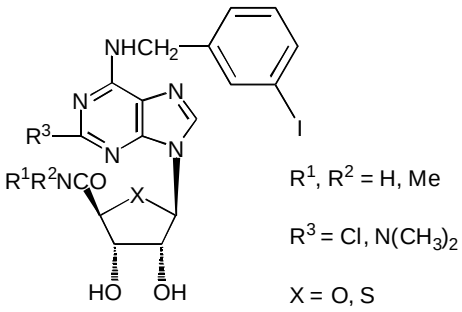



**Inhibition of GABA shunt enzymes' activity by 4-hydroxybenzaldehyde derivatives** **pp 592–595**
Yun-Hai Tao, Zheng Yuan, Xiao-Qiao Tang, Hui-Bi Xu and Xiang-Liang Yang*

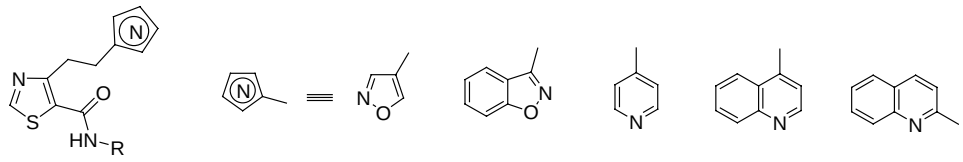


Possible mechanism of the inhibition of GABA-T by HBA and HBM.

**Conversion of $A_3$ adenosine receptor agonists into selective antagonists by modification of the 5′-ribofuran-uronamide moiety** **pp 596–601**
Zhan-Guo Gao, Bhalchandra V. Joshi, Athena M. Klutz, Soo-Kyung Kim, Hyuk Woo Lee, Hea Ok Kim, Lak Shin Jeong and Kenneth A. Jacobson*

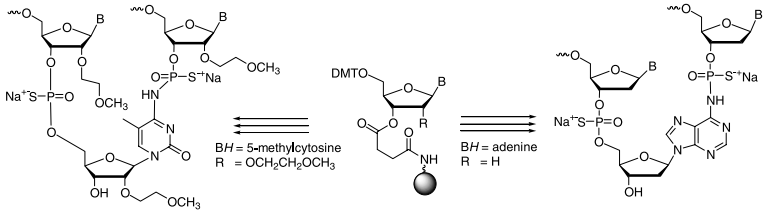


**_N_-(Aryl)-4-(azolylethyl)thiazole-5-carboxamides: Novel potent inhibitors of VEGF receptors I and II** **pp 602–606**
Alexander S. Kiselyov,* Evgueni Piatnitski, Marina Semenova and Victor V. Semenov



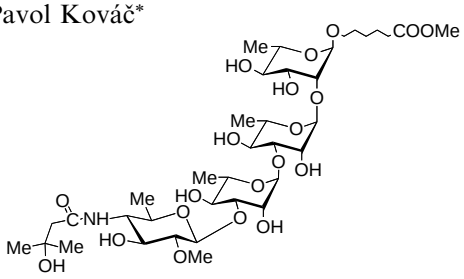
Novel potent derivatives of 4-(azolylethyl)thiazole-5-carboxamides are described as inhibitors of vascular endothelial growth factor receptor II (VEGFR-2). Many compounds display VEGFR-2 inhibitory activity reaching $IC_{50} < 100$ nM in both enzymatic and cell-based phosphorylation assays. The compounds also inhibit the related tyrosine kinase, VEGFR-1, with similar potencies.

**Characterization of high molecular weight impurities in synthetic phosphorothioate oligonucleotides** **pp 607–614**
Christine Kurata, Kym Bradley, Hans Gaus, Nhuy Luu, Isaiah Cedillo, Vasulinga T. Ravikumar, Kent Van Sooy, James V. McArdle and Daniel C. Capaldi*



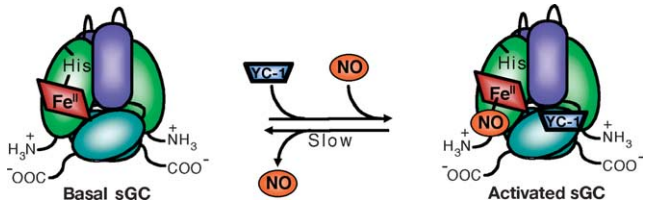

Phosphorothioate oligonucleotides manufactured by standard phosphoramidite techniques using nucleoside-loaded supports contain high molecular weight impurities of the type shown. These impurities are avoided if a novel universal solid support is used.

**Synthesis of the tetrasaccharide side chain of the major glycoprotein of the *Bacillus anthracis* exosporium** **pp 615–617**
Rina Saksena, Roberto Adamo and Pavol Kováč*

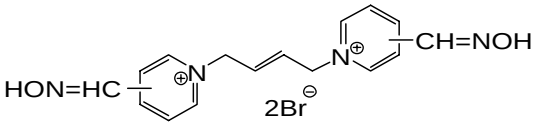


Chemical synthesis of tetrasaccharide **20** is described. The NMR data recorded for **20** confirm structure assigned to the corresponding reducing tetrasaccharide isolated from the major glycoprotein of *Bacillus anthracis* exosporium.

**The design and synthesis of YC-1 analogues as probes for soluble guanylate cyclase** **pp 618–621**
Kirk W. Hering, Jennifer D. Artz, William H. Pearson and Michael A. Marletta*

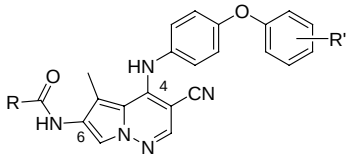


**Synthesis of the novel series of bispyridinium compounds bearing (*E*)-but-2-ene linker and evaluation of their reactivation activity against chlorpyrifos-inhibited acetylcholinesterase** **pp 622–627**
Kamil Musilek, Kamil Kuca,* Daniel Jun, Vlastimil Dohnal and Martin Dolezal



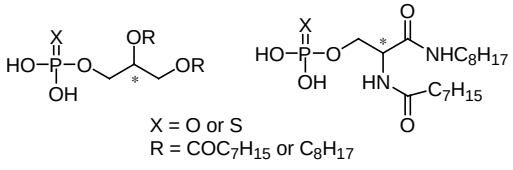

A series of novel bisquaternary reactivators of acetylcholinesterase (AChE) with (*E*)-but-2-ene connecting chain was synthesized and evaluated on chlorpyrifos-inhibited AChE with promising results.

**Pyrrolopyridazine MEK inhibitors** **pp 628–632**
Zhong Chen,* Soong-Hoon Kim, Stephanie A. Barbosa, Tram Huynh, David R. Tortolani, Kenneth J. Leavitt, Donna D. Wei, Veeraswamy Manne, Carolyn S. Ricca, Johnni Gullo-Brown, Michael A. Poss, Wayne Vaccaro and Mark E. Salvati



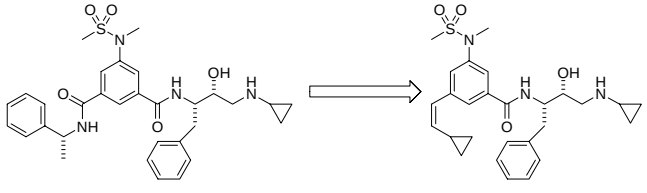

The synthesis and SAR of a series of pyrrolopyridazine MEK inhibitors are reported. Optimal activity was achieved by incorporation of a 4-phenoxyaniline substituent at C4 and an acylated amine at C6.

**Synthesis and pharmacological evaluation of second-generation phosphatidic acid derivatives as lysophosphatidic acid receptor ligands** **pp 633–640**
Gangadhar G. Durgam, Ryoko Tsukahara, Natalia Makarova, Michelle D. Walker, Yuko Fujiwara, Kathryn R. Pigg, Daniel L. Baker, Vineet M. Sardar, Abby L. Parrill, Gabor Tigyi and Duane D. Miller*

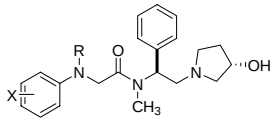



**Second-generation PA analogs**

**Conformationally biased P3 amide replacements of β-secretase inhibitors** **pp 641–644**
Shawn J. Stachel,* Craig A. Coburn, Thomas G. Steele, Min-Chi Crouthamel, Beth L. Pietrak, Ming-Tain Lai, M. Katharine Holloway, Sanjeev K. Munshi, Samuel L. Graham and Joseph P. Vacca

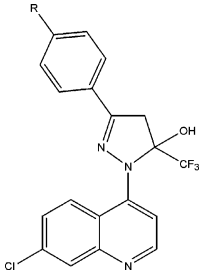


**Novel phenylamino acetamide derivatives as potent and selective κ opioid receptor agonists** **pp 645–648**
Guo-Hua Chu,* Minghua Gu, Joel A. Cassel, Serge Belanger, Gabriel. J. Stabley, Robert N. DeHaven, Nathalie Conway-James, Mike Koblish, Patrick J. Little, Diane L. DeHaven-Hudkins and Roland E. Dolle

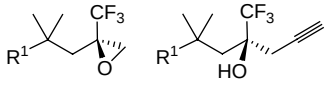



**Antimalarial activity of 4-(5-trifluoromethyl-1*H*-pyrazol-1-yl)-chloroquine analogues** **pp 649–653**
Wilson Cunico, Cleber A. Cechinel, Helio G. Bonacorso, Marcos A. P. Martins, Nilo Zanatta, Marcus V. N. de Souza, Isabela O. Freitas, Rodrigo P. P. Soares and Antoniana U. Krettli*

The antimalarial activity of 4,5-dihydropyrazole and pyrazole chloroquine analogues is reported.




**A concise asymmetric route for the synthesis of a novel class of glucocorticoid mimetics containing a trifluoromethyl-substituted alcohol** **pp 654–657**
Thomas W. Lee,* John R. Proudfoot and David S. Thomson

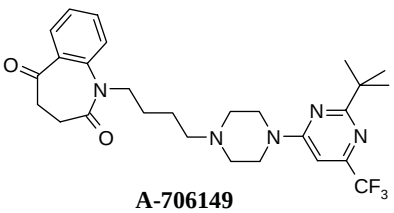



**2** **3**

An asymmetric route involving intermediates **2** and **3** was developed for the synthesis of a class of novel glucocorticoid receptor ligand derivatives.

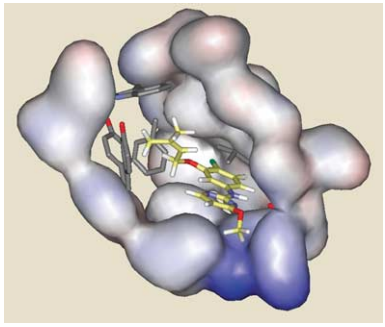
**Synthesis and SAR of highly potent and selective dopamine $D_3$-receptor antagonists: Quinolin(di)one and benzazepin(di)one derivatives** **pp 658–662**
Hervé Geneste,* Gisela Backfisch, Wilfried Braje, Jürgen Delzer, Andreas Haupt, Charles W. Hutchins, Linda L. King, Wilfried Lubisch, Gerd Steiner, Hans-Jürgen Teschendorf, Liliane Unger and Wolfgang Wernet

The synthesis and SAR of novel and selective dopamine $D_3$-receptor antagonists based on a 3,4-dihydro-1*H*-quinolin-2-one, a 1,3,4,5-tetrahydro-benzo[*b*]azepin-2-one, 1*H*-quinoline-2,4-dione or a 3,4-dihydro-1*H*-benzo[*b*]azepine-2,5-dione scaffold are discussed. **A-706149** (2.15 mg/kg, po) antagonizes PD 128907-induced huddling deficits in rat, a social interaction paradigm.

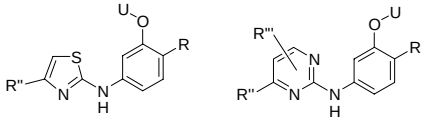



**A-706149**

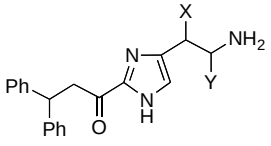
**Computer-aided design of non-nucleoside inhibitors of HIV-1 reverse transcriptase** **pp 663–667**
William L. Jorgensen,* Juliana Ruiz-Caro, Julian Tirado-Rives, Aravind Basavapathruni, Karen S. Anderson and Andrew D. Hamilton



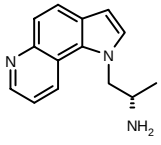
**Optimization of diarylamines as non-nucleoside inhibitors of HIV-1 reverse transcriptase** **pp 668–671**
Juliana Ruiz-Caro, Aravind Basavapathruni, Joseph T. Kim, Christopher M. Bailey, Ligong Wang, Karen S. Anderson,* Andrew D. Hamilton and William L. Jorgensen*




**Side-chain modified analogues of histaprodifen: Asymmetric synthesis and histamine $H_1$-receptor activity** **pp 672–676**
Rameshwar Patil, Sigurd Elz* and Oliver Reiser*



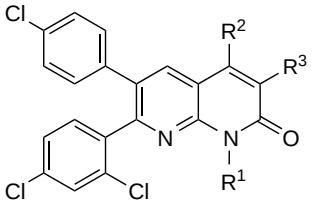

**Pyrrolo(iso)quinoline derivatives as 5-$HT_{2C}$ receptor agonists** **pp 677–680**
David R. Adams, Jonathan M. Bentley, Karen R. Benwell, Michael J. Bickerdike, Corinna D. Bodkin, Ian A. Cliffe, Colin T. Dourish, Ashley R. George, Guy A. Kennett, Antony R. Knight, Craig S. Malcolm, Howard L. Mansell,* Anil Misra, Kathleen Quirk, Jonathan R. A. Roffey and Steven P. Vickers



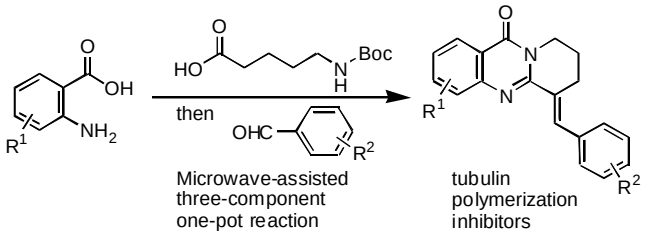

A series of 1-(1-pyrrolo(iso)quinolinyl)-2-propylamines was prepared and evaluated as 5-$HT_{2C}$ receptor agonists for the treatment of obesity.

**Synthesis of functionalized 1,8-naphthyridinones and their evaluation as novel, orally active CB1 receptor inverse agonists** **pp 681–685**
John S. Debenham,* Christina B. Madsen-Duggan, Thomas F. Walsh, Junying Wang, Xinchun Tong, George A. Doss, Julie Lao, Tung M. Fong, Marie-Therese Schaeffer, Jing Chen Xiao, Cathy R.-R. C. Huang, Chun-Pyn Shen, Yue Feng, Donald J. Marsh, D. Sloan Stribling, Lauren P. Shearman, Alison M. Strack, D. Euan MacIntyre, Lex H. T. Van der Ploeg and Mark T. Goulet

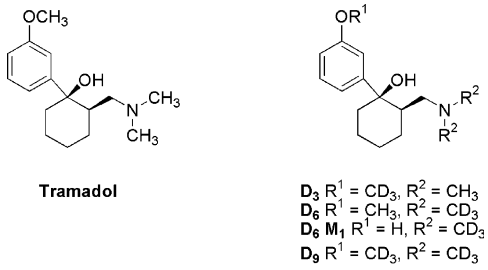
The synthesis, structure–activity relationship, and biological evaluation of a new class of 1,8-naphthyridinone CB1 receptor specific inverse agonists are described.




**Privileged structure-based quinazolinone natural product-templated libraries: Identification of novel tubulin polymerization inhibitors** **pp 686–690**
Ji-Feng Liu,* Christopher J. Wilson, Ping Ye, Kevin Sprague, Katie Sargent, Ying Si, Galina Beletsky, Daniel Yohannes and Shi-Chung Ng

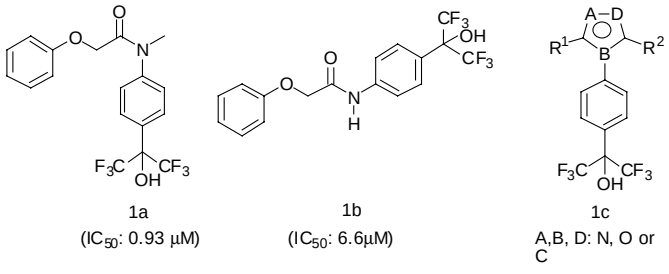



**Derivatives of tramadol for increased duration of effect** **pp 691–694**
Liming Shao,* Craig Abolin, Michael C. Hewitt, Patrick Koch and Mark Varney

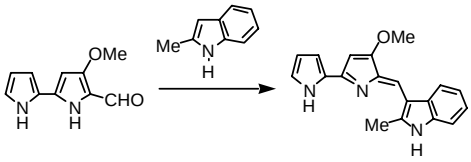



**Design and synthesis of heterocyclic malonyl-CoA decarboxylase inhibitors** **pp 695–700**
Jie-Fei Cheng,* Mi Chen, Bin Liu, Zheng Hou, Thomas Arrhenius and Alex M. Nadzan

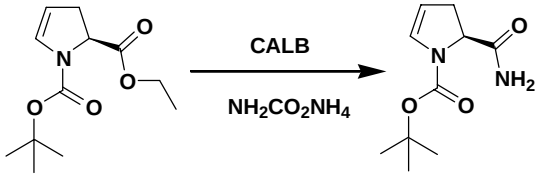
Based on the initial HTS hit **1a**, a series of heterocycles (**1c**) such as isoxazole and imidazoles designed to mimic the amide conformation was synthesized and SAR studies werre performed.



**Indoloprodigiosins from the C-10 bipyrrolic precursor: New antiproliferative prodigiosin analogs** **pp 701–704**
Carmen M. Baldino,* Jonathan Parr, Christopher J. Wilson, Shi-Chung Ng, Daniel Yohannes and Harry H. Wasserman*

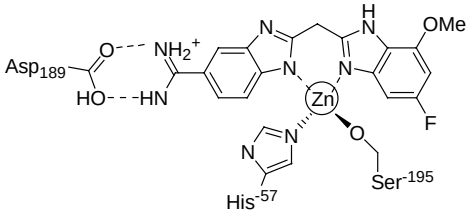



**Biocatalytic ammonolysis of (5*S*)-4,5-dihydro-1*H*-pyrrole-1,5-dicarboxylic acid, 1-(1,1-dimethylethyl)-5-ethyl ester: Preparation of an intermediate to the dipeptidyl peptidase IV inhibitor Saxagliptin** **pp 705–709**
Iqbal Gill* and Ramesh Patel



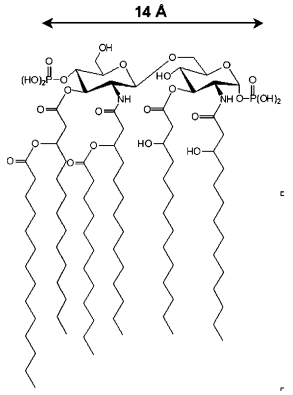

**Generation of potent coagulation protease inhibitors utilizing zinc-mediated chelation** **pp 710–713**
Wendy B. Young,* Paul Sprengeler, William D. Shrader, Yong Li, Roopa Rai, Erik Verner, Thomas Jenkins, Paul Fatheree, Aleksandr Kolesnikov, James W. Janc, Lynne Cregar, Kyle Elrod and Brad Katz

Inhibition of coagulation proteases such as thrombin, fXa, and fVIIa has been a focus of ongoing research to produce safe and effective antithrombotic agents. Herein, we describe a unique zinc-mediated chelation strategy to streamline the discovery of potent inhibitors of fIIa, fXa, and fVIIa. SAR studies that led to the development of selective inhibitors of fXa will also be detailed.



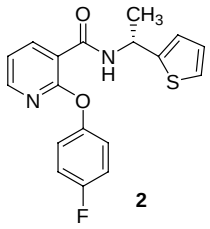

**Molecular modeling analysis of the interaction of novel bis-cationic ligands with the lipid A moiety of lipopolysaccharide** **pp 714–717**
Jian-Xin Guo, Stewart J. Wood, Sunil A. David * and Gerald H. Lushington *

The lipopolysaccharide pharmacophore, dominated by cationic phosphate centers but also comprising hydrophobic and H-bond acceptor and donor sites.



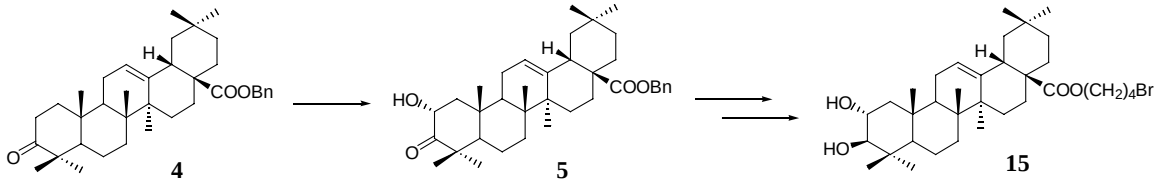
**A new chemical tool for exploring the role of the PDE4D isozyme in leukocyte function** **pp 718–721**
Robert J. Chambers,* Kristin Abrams, Tessa A. Castleberry, John B. Cheng, Douglas A. Fisher, Ajith V. Kamath, Anthony Marfat, David O. Nettleton, Joann D. Pillar, Eben D. Salter, Alissa L. Sheils, John T. Shirley, Claudia R. Turner, John P. Umland and Kelvin T. Lam

Nicotinamide (**2**) is a potent and selective inhibitor of the PDE4D isozyme and as a chemical tool selectively blocks eosinophil mediator release and chemotaxis thus linking the role of PDE4D to eosinophil function.



**2**

**Pentacyclic triterpenes. Part 2: Synthesis and biological evaluation of maslinic acid derivatives as glycogen phosphorylase inhibitors** **pp 722–726**
Xiaoan Wen, Pu Zhang, Jun Liu, Luyong Zhang, Xiaoming Wu, Peizhou Ni and Hongbin Sun*

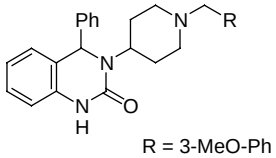


**4** **5** **15**

( $IC_{50}$ = 7 μM)

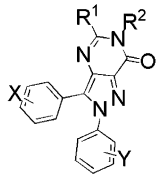
The synthesis of a series of maslinic acid derivatives is described and their effect on rabbit muscle glycogen phosphorylase a evaluated. Within this series of compounds, **15** ($IC_{50}$ = 7 μM) is the most potent GPa inhibitor.

**A novel class of sodium/calcium exchanger inhibitors: Design, synthesis, and structure–activity relationships of 4-phenyl-3-(piperidin-4-yl)-3,4-dihydro-2(1*H*)-quinazolinone derivatives** **pp 727–730**
Hirohiko Hasegawa,* Masami Muraoka, Kazuki Matsui and Atsuyuki Kojima

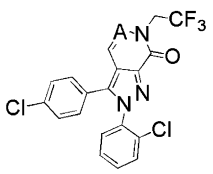


R = 3-MeO-Ph

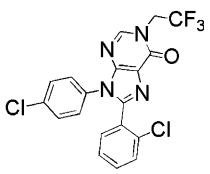
**New bicyclic cannabinoid receptor-1 ($CB_1$-R) antagonists** **pp 731–736**
Philip A. Carpino,* David A. Griffith, Subas Sakya, Robert L. Dow, Shawn C. Black, John R. Hadcock, Philip A. Iredale, Dennis O. Scott, Michael W. Fichtner, Colin R. Rose, Robert Day, Joseph Dibrino, Mary Butler, Demetria B. DeBartolo, Darrin Dutcher, Denise Gautreau, Jeff S. Lizano, Rebecca E. O'Connor, Michelle A. Sands, Dawn Kelly-Sullivan and Karen M. Ward



**2-4**, $hCB_1$-R Ki's = 0.2 - 38 nM



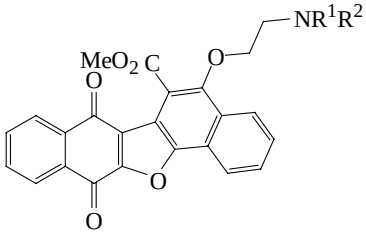
**5** and **6**, A = C or N, $hCB_1$-R Ki = 1 - 8 nM



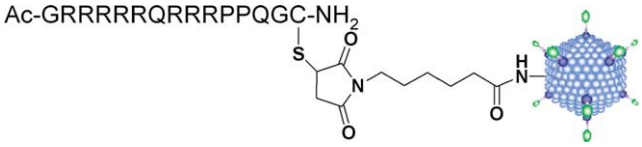
**7**, $hCB_1$-R Ki = 1 nM

**Naphthofuroquinone derivatives: Inhibition of receptor tyrosine kinases** **pp 737–742**
Kee-In Lee, Youmie Park, Su-Jin Park, Jung-Hwan Hwang, Sung-Jin Lee, Gun-Do Kim, Woo-Kyu Park, Sunghou Lee, Daeyoung Jeong, Jae-Yang Kong, Hee-Kyoung Kang and Heeyeong Cho *

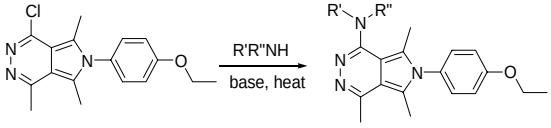
A series of dinaphtho[1,2-*b*;2′,3′-*d*]furan-7,12-dione derivatives were synthesized and evaluated for inhibitory activities against receptor tyrosine kinases. The naphthofuroquinone compounds with dialkylaminoethoxy group at C(5)-position (**7**, **8**, **10**, and **11**) manifested strong inhibitory activities against epidermal growth factor receptor and vascular endothelial growth factor receptor. Docking study of **11** with EGFR was also performed.




**Design and synthesis of a Tat-related gene transporter: A tool for carrying the adenovirus vector into cells** **pp 743–745**
Shinya Kida, Mitsuko Maeda, Keiko Hojo, Yusuke Eto, Jian-Qing Gao, Shinnosuke Kurachi, Hiroyuki Mizuguchi, Takao Hayakawa, Tadanori Mayumi, Shinsaku Nakagawa and Koichi Kawasaki *




**Expedited SAR study of high-affinity ligands to the $\alpha_2\delta$ subunit of voltage-gated calcium channels: Generation of a focused library using a solution-phase Sn2Ar coupling methodology** **pp 746–749**
Chixu Chen,* Brian Stearns, Tao Hu, Naomi Anker, Angelina Santini, Jeannie M. Arruda, Brian T. Campbell, Purabi Datta, Jayashree Aiyar and Benitio Munoz

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*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

## COVER

Computer-aided design has been used to guide the efficient development of new non-nucleoside inhibitors of HIV-1 reverse transcriptase. Lead compounds were provided by the ligand-growing program *BOMB* and optimized with guidance from free-energy perturbation calculations. It was possible to progress rapidly a 30-μM lead from an anti-HIV cell-based assay to yield the illustrated 10-nM inhibitor. [Jorgensen, W. L.; Ruiz-Caro, J.; Tirado-Rives, J.; Basavapathruni, A.; Anderson, K. S.; Hamilton, A. D. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 663.]



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