

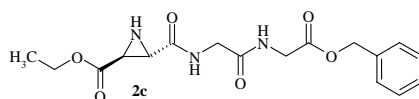
Contents

ARTICLES

Screening of electrophilic compounds yields an aziridinyl peptide as new active-site directed SARS-CoV main protease inhibitor

pp 5365–5369

Erika Martina, Nikolaus Stiefl, Björn Degel, Franziska Schulz, Alexander Breuning, Markus Schiller, Radim Vicik, Knut Baumann, John Ziebuhr and Tanja Schirmeister*



The inhibition of SARS-CoV main protease by the aziridinyl peptide **2c** is described.



Factors affecting the protease activity of venom from jellyfish *Rhopilema esculentum* Kishinouye

pp 5370–5374

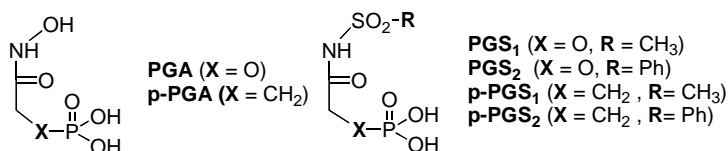
Cuiping Li, Huahua Yu, Song Liu, Rong Xing, Zhanyong Guo and Pengcheng Li*

In this paper, protease activity of protein isolated from jellyfish *Rhopilema esculentum* Kishinouye was determined by the method of Folin-phenol. The protease activity was affected by temperature, pH values, glycerol, divalent metal cations, *O*-phenanthroline, and EDTA. 0.5% *O*-phenanthroline and 1% glycerol could significantly inhibit protease activity.

***N*-Sulfonyl hydroxamate derivatives as inhibitors of class II fructose-1,6-diphosphate aldolase**

pp 5375–5377

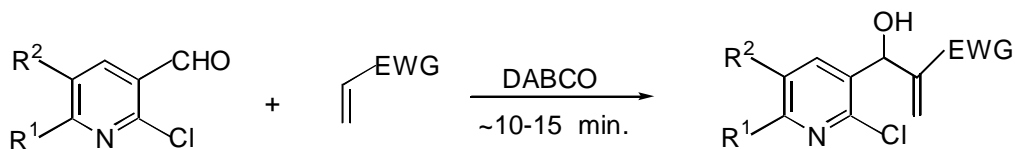
Sabine Gavalda, Rémi Braga, Chantal Dax, Alain Vigroux and Casimir Blonski*



Anti-malarial activity of Baylis–Hillman adducts from substituted 2-chloronicotinaldehydes

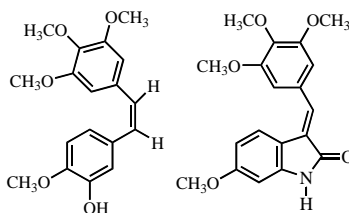
pp 5378–5381

P. Narender, U. Srinivas, B. Gangadasu, Sukla Biswas* and V. Jayathirtha Rao*

**Conformationally restricted analogs of Combretastatin A-4 derived from SU5416**

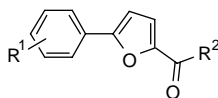
pp 5382–5385

Pui-Kai Li,* Zili Xiao, Zhigen Hu, Bulbul Pandit, Yanjun Sun, Dan L. Sackett, Karl Werbovetz, Andrew Lewis and Jayasekar Johnsamuel

**Metalloform-selective inhibition: Synthesis and structure–activity analysis of Mn(II)-form-selective inhibitors of *Escherichia coli* methionine aminopeptidase**

pp 5386–5391

Qing-Qing Huang, Min Huang, Fa-Jun Nan* and Qi-Zhuang Ye*

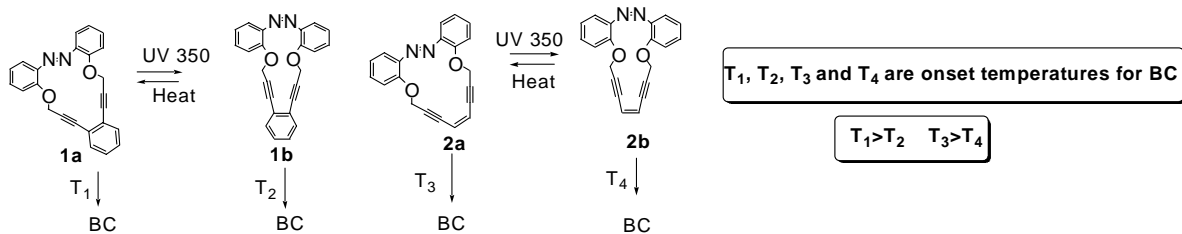


A new series of analogs of 5-phenylfuran-2-carboxylic acid was prepared and subsequently evaluated on Co(II)-, Mn(II)-, Ni(II)-, and Fe(II)-forms of *Escherichia coli* MetAP, in order to define the structural elements responsible for their potency and metalloform selectivity.

Photoisomerization as a trigger for Bergman cyclization: Synthesis and reactivity of azoenediynes

pp 5392–5396

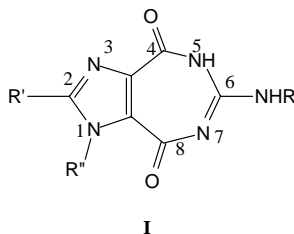
Moumita Kar, Amit Basak* and Manish Bhattacharjee



Synthesis and in vitro anti-hepatitis B and C virus activities of ring-expanded ('fat') nucleobase analogues containing the imidazo[4,5-*e*][1,3]diazepine-4,8-dione ring system

pp 5397–5401

Peng Zhang, Ning Zhang, Brent E. Korba and Ramachandra S. Hosmane*

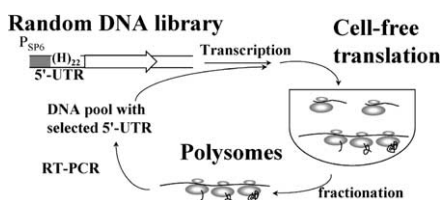


The synthesis and in vitro anti-HBV and anti-HCV activities of a number of ring-expanded ('fat') nucleobases containing the imidazo[4,5-*e*][1,3]diazepine-4,8-dione ring system (**I**) have been reported.

**Selection of 5'-untranslated sequences that enhance initiation of translation in a cell-free protein synthesis system from wheat embryos**

pp 5402–5406

Nami Kamura, Tatsuya Sawasaki, Yuko Kasahara, Kazuyuki Takai and Yaeta Endo*

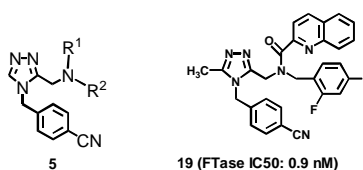


Two novel sequences that enhance translation of downstream open reading frames were obtained by random library selection through isolation of polysomes generated in vitro.

**Novel triazole based inhibitors of Ras farnesyl transferase**

pp 5407–5411

Ashis K. Saha,* Li Liu, Richard Simoneaux, Bart DeCorte, Christophe Meyer, Stacy Skrzat, Henry J. Breslin, Michael J. Kukla and Dave W. End



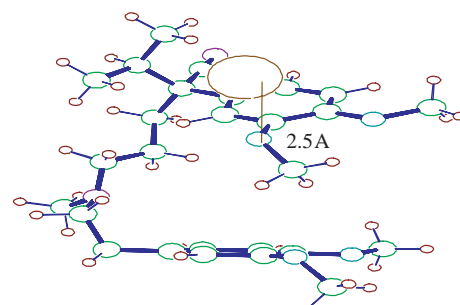
A novel series of potent inhibitors of Ras farnesyl transferase possessing a 1,2,4-triazole pharmacophore (**5**) is described. These inhibitors were discovered from a parallel synthesis effort and were subsequently optimized to in vitro IC₅₀ value of less than 1 nM (**19**).

Pharmacophoric features and Ca²⁺ ion holding capacity of verapamil

pp 5412–5415

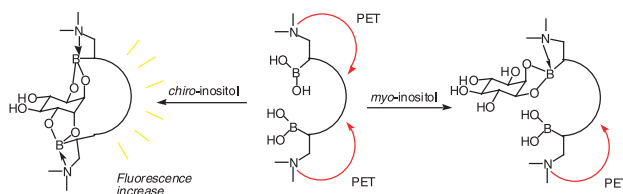
Anamika Awasthi and Arpita Yadav*

Ab initio Hartree–Fock calculations have been performed to study unprotonated and protonated forms of verapamil. The study predicts that huge conformational change as well as deprotonation is required before the drug is capable of holding Ca²⁺ ion.



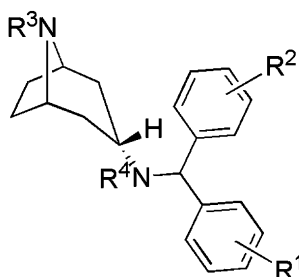
Specific sensing between inositol epimers by a bis(boronate)

pp 5416–5418

Charles W. Gray, Jr., Leland L. Johnson, Jr., Brian T. Walker, Mark C. Sleeve*,
A. Stewart Campbell, Robert Plourde and Todd A. Houston***N-8-Substituted benzotropinamine analogs as selective dopamine transporter ligands**

pp 5419–5423

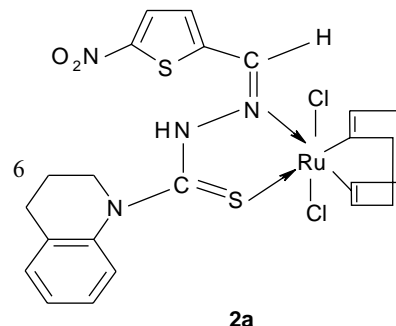
Peter Grundt, Theresa A. Kopajtic, Jonathan L. Katz and Amy Hauck Newman*

**Synthesis, spectral studies and in vitro assessment for antiamoebic activity of new cyclooctadiene ruthenium(II) complexes with 5-nitrothiophene-2-carboxaldehyde thiosemicarbazones**

pp 5424–5428

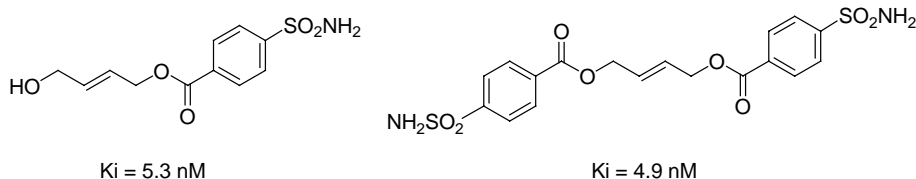
Shailendra Singh, Fareeda Athar and Amir Azam*

We report here the synthesis, characterization and in vitro antiamoebic activity of 5-nitrothiophene-2-carboxaldehyde thiosemicarbazones (TSC), **1–5**, and their complexes [Ru(η^4 -C₈H₁₂)(TSC)Cl₂] **1a–5a**. The most promising among these compounds is Ru(II) complex **2a** having 1,2,3,4-tetrahydroquinoline as N⁴ substitution.

**Synthesis and structure–activity relationships of novel benzene sulfonamides with potent binding affinity for bovine carbonic anhydrase II**

pp 5429–5433

Sally-Ann Poulsen*, Laurent F. Bornaghi and Peter C. Healy

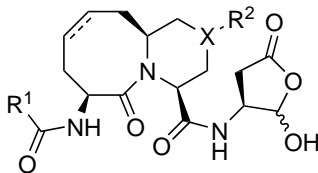


The synthesis and structure–activity relationships of a novel series of mono- and bis- benzene sulfonamides with potent binding affinity for bovine carbonic anhydrase II are reported.

Synthesis and evaluation of novel 8,6-fused bicyclic peptidomimetic compounds as interleukin-1 β converting enzyme inhibitors

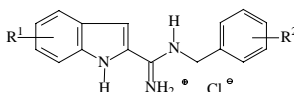
pp 5434–5438

Steven V. O'Neil,* Yili Wang, Michael C. Laufersweiler, Kofi A. Oppong, David L. Soper, John A. Vos, Christopher D. Ellis, Mark W. Baize, Gregory K. Bosch, Amy N. Fancher, Wei Lu, Maureen K. Suchanek, Richard L. Wang, Biswanath De and Thomas P. Demuth, Jr.

**Indole-2-carboxamidines as novel NR2B selective NMDA receptor antagonists**

pp 5439–5441

István Borza,* Sándor Kolok, Györgyi Ignácz-Szendrei, István Greiner, Gábor Tárkányi, Kornél Galgóczy, Csilla Horváth, Sándor Farkas and György Domány

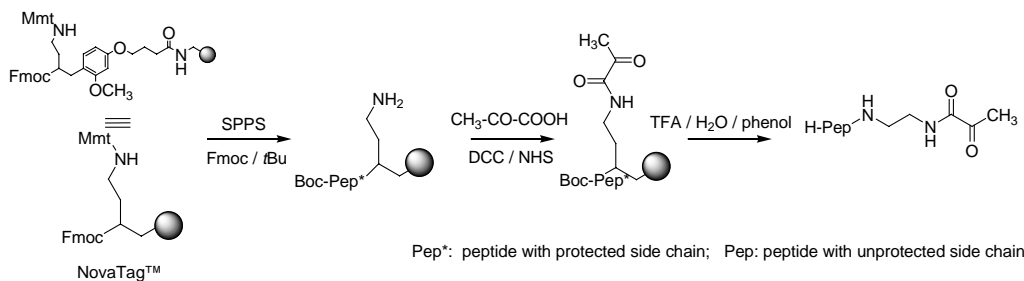


A novel series of indole-2-carboxamidines derivatives was prepared and identified as NR2B selective NMDA receptor antagonists. The influence of the substituents on the indole skeleton as well as the substitution of the benzyl moiety on the biological activity of the compounds was studied. Compound **5a** was po active in the formalin test in mouse.

Efficient synthesis of C-terminal modified peptide ketones for chemical ligations

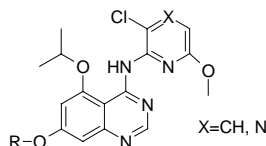
pp 5442–5445

Philippe Marceau, Corinne Buré and Agnès F. Delmas*

**New heterocyclic analogues of 4-(2-chloro-5-methoxyanilino)quinazolines as potent and selective c-Src kinase inhibitors**

pp 5446–5449

Bernard Barlaam,* Mike Fennell, Hervé Germain, Tim Green, Laurent Hennequin, Rémy Morgentin, Annie Olivier, Patrick Plé, Michel Vautier and Gerard Costello



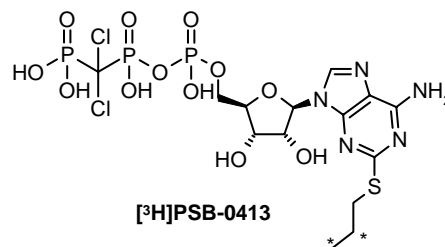
5,7-Disubstituted 4-heteroarylaminquinazolines of the type above have been synthesised and evaluated as c-Src kinase inhibitors. Highly potent inhibition, high selectivity and physical properties suitable for oral dosing were achieved with this series.

Synthesis and preliminary evaluation of [³H]PSB-0413, a selective antagonist radioligand for platelet P2Y₁₂ receptors

pp 5450–5452

Ali El-Tayeb, Kerstin J. Griessmeier and Christa E. Müller*

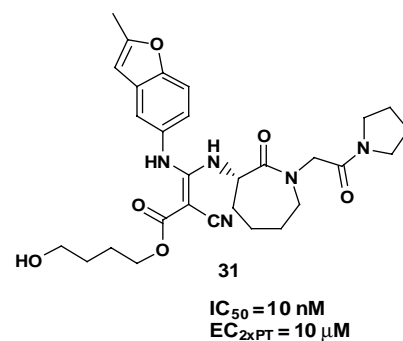
The preparation of the first selective antagonist radioligand for P2Y₁₂ receptors is reported with a high specific radioactivity of 74 Ci/mmol. A K_D value of 4.57 nM and a B_{max} value of 7.66 pmol/mg of protein were determined for P2Y₁₂ receptors natively expressed in human blood platelet membranes.



Ketene aminal-based lactam derivatives as a novel class of orally active FXa inhibitors

pp 5453–5458

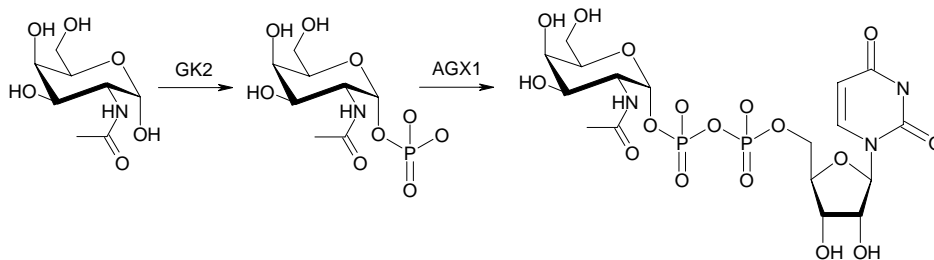
Yan Shi,* Jing Zhang, Philip D. Stein, Mengxiao Shi, Stephen P. O'Connor, Sharon N. Bisaha, Chi Li, Karnail S. Atwal, Gregory S. Bisacchi, Doree Sitkoff, Andrew T. Pudzianowski, Eddie C. Liu, Karen S. Hartl, Steven M. Seiler, Sonia Youssef, Thomas E. Steinbacher, William A. Schumacher, Alan R. Rendina, Jeffrey M. Bozarth, Tara L. Peterson, Ge Zhang and Robert Zahler



Two-step enzymatic synthesis of UDP-*N*-acetylgalactosamine

pp 5459–5462

Vanessa Bourgeaux, Friedrich Piller and Véronique Piller*

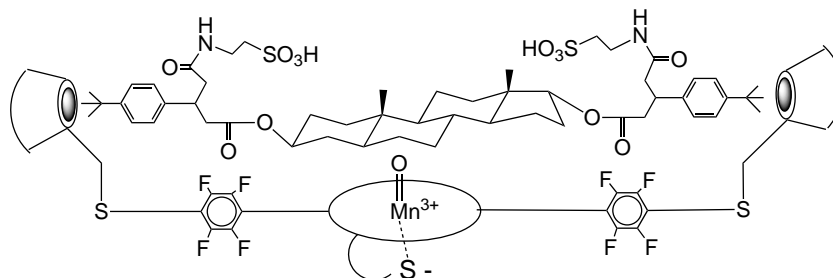


UDP-GalNAc has been synthesised with high yield from GalNAc, UTP and ATP using recombinant human GalNAc kinase GK2 and UDP-GalNAc pyrophosphorylase AGX1. The method proved to be applicable to UDP-*N*-azidoacetylgalactosamine synthesis.

A thiolate ligand on a cytochrome P-450 mimic permits the use of simple environmentally benign oxidants for biomimetic steroid hydroxylation in water

pp 5463–5466

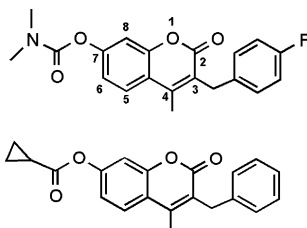
Zhenglai Fang and Ronald Breslow*



Identification of coumarin derivatives as a novel class of allosteric MEK1 inhibitors

pp 5467–5473

Shulin Han, Vicki Zhou, Shifeng Pan, Yi Liu, Michael Hornsby,
Daniel McMullan, Heath E. Klock, Justin Haugen, Scott A. Lesley,
Nathanael Gray, Jeremy Caldwell and Xiang-ju Gu*

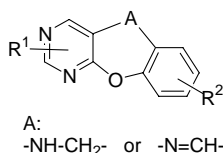


The coumarin derivatives were identified as a novel class of allosteric MEK1 inhibitors.

Pyrimido-oxazepine as a versatile template for the development of inhibitors of specific kinases

pp 5474–5477

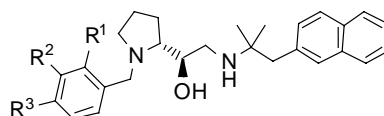
Weitao Pan, Hu Liu,* Yong-Jiang Xu, Xin Chen, Ki Hwan Kim, Daniel L. Milligan,
John Columbus, Yaron R. Hadari, Paul Kussie, Wai C. Wong and Marc Labelle



The development of pyrimido-oxazepine based inhibitors for Aurora and FLT-3 is reported.

Discovery of novel 1-arylmethyl pyrrolidin-2-yl ethanol amines as calcium-sensing receptor antagonists pp 5478–5482

Ashvinikumar V. Gavai,* Roy J. Vaz, Amarendra B. Mikkilineni, Jacques Y. Roberge,
Yalei Liu, R. Michael Lawrence, James R. Corte, Wu Yang, Mark Bednarz,
John K. Dickson, Jr., Zhengping Ma, Ramakrishna Seethala and Jean H. M. Feyen

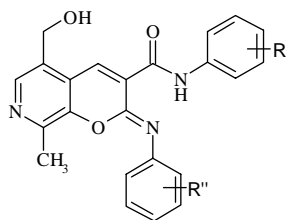


The synthesis and structure–activity relationship study of a novel family of calcium-sensing receptor antagonists are reported.

Synthesis and antimicrobial activity of 5-hydroxymethyl-8-methyl-2-(N-arylimino)-pyrano[2,3-c]pyridine-3-(N-aryl)-carboxamides

pp 5483–5487

Irina O. Zhuravel', Sergiy M. Kovalenko, Alexandre V. Ivachtchenko,*
Konstantin V. Balakin and Victor V. Kazmirchuk



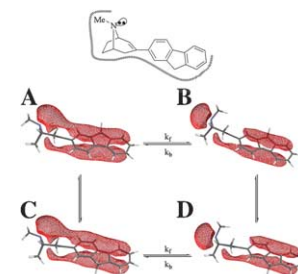
Synthesis, antibacterial, and antifungal activities of novel 2H-pyrano[2,3-c]pyridines.

Synthesis and monoamine transporter affinity of 3-aryl substituted trop-2-enes

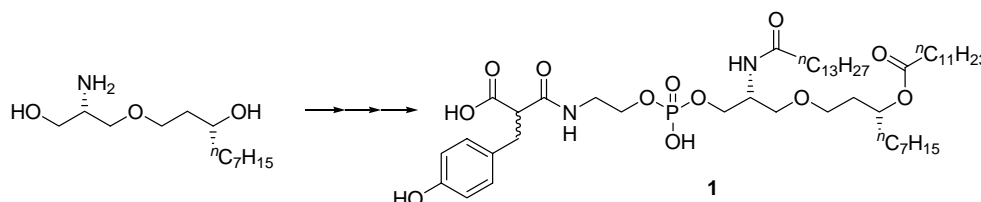
pp 5488–5493

Alekszej Krunic, S. V. Santhana Mariappan,* Marteen E. A. Reith and William J. Dunn, III

A 3-aryl-trop-2-ene ligand shown in the tentative binding pocket of a human monoamine transporter. Conformational states A–D are dependent on the selection of the aromatic substituent at C3. The red colored electrostatic potential maps reveal the electron rich regions of A–D.

**Toll-like receptor 2 antagonists. Part 1: Preliminary SAR investigation of novel synthetic phospholipids** pp 5494–5498

Mark R. Spyvee,* Huiming Zhang, Lynn D. Hawkins and Jesse C. Chow

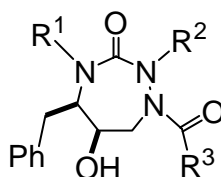


Phospholipid compound **1** was discovered as a novel antagonist of toll-like receptor 2 signaling. Synthesis and biological properties are described for **1** and eight related analogues.

Synthesis and activity of *N*-acyl azacyclic urea HIV-1 protease inhibitors with high potency against multiple drug resistant viral strains

pp 5499–5503

Chen Zhao,* Hing L. Sham, Minghua Sun, Vincent S. Stoll, Kent D. Stewart, Shuqun Lin, Hongmei Mo, Sudthida Vasavanonda, Ayda Saldivar, Chang Park, Edith J. McDonald, Kennan C. Marsh, Larry L. Klein, Dale J. Kempf and Daniel W. Norbeck

**II**, *N*-Acyl Aza-cyclic Urea**Preparation of human Melanocortin-4 receptor agonist libraries:**

pp 5504–5508

Linear peptides X-Y-DPhe⁷-Arg⁸-Trp(or 2-Nal)⁹-Z-NH₂

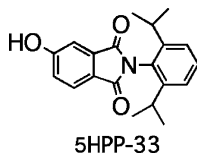
Adrian Wai-Hing Cheung,* Lida Qi, Vijay Gore, Xin-Jie Chu, David Bartkovitz, Grazyna Kurylko, Joseph Swistok, Waleed Danho, Li Chen and Keith Yagaloff

Two libraries of hMC4R agonists, X-Y-DPhe⁷-Arg⁸-2-Nal⁹-Z-NH₂ and X-Y-DPhe⁷-Arg⁸-Trp⁹-Z-NH₂, totaling 185 peptides were prepared using Irri radiofrequency tagging technology and Argonaut Quest 210 Synthesizer, where **X** stands for N-caps, **Y** for His⁶ surrogates, and **Z** for Gly¹⁰ surrogates. As a result of this study, pentapeptides with Trp were found to be more hMC4R potent than the corresponding 2-Nal analogs, novel N-caps and Gly surrogates were identified, and 19 new peptides which are potent hMC4R agonists (EC₅₀ 1–15 nM) and selective against hMC1R were discovered.

Angiogenesis inhibitors derived from thalidomide

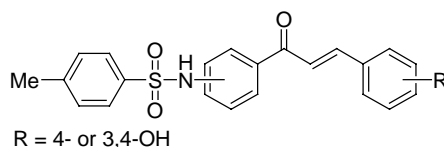
pp 5509–5513

Tomomi Noguchi, Haruka Fujimoto, Hiroko Sano, Atsushi Miyajima, Hiroyuki Miyachi and Yuichi Hashimoto*

**Sulfonamide chalcone as a new class of α -glucosidase inhibitors**

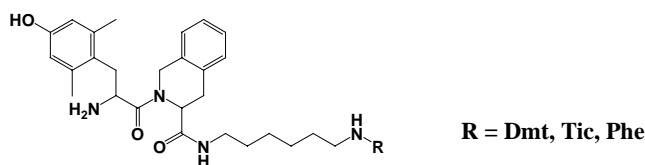
pp 5514–5516

Woo Duck Seo, Jin Hyo Kim, Jae Eun Kang, Hyung Won Ryu, Marcus J. Curtis-Long, Hyun Sun Lee, Min Suk Yang and Ki Hun Park*

**New series of potent δ -opioid antagonists containing the H-Dmt-Tic-NH-hexyl-NH-R motif**

pp 5517–5520

Tingyou Li, Kimitaka Shiotani, Anna Miyazaki, Yoshio Fujita, Yuko Tsuda, Akihiro Ambo, Yusuke Sasaki, Yunden Jinsmaa, Ewa Marczak, Sharon D. Bryant, Lawrence H. Lazarus* and Yoshio Okada*



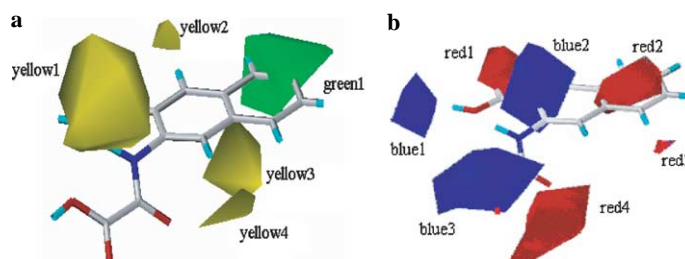
δ -Receptor antagonism: $pA_2 = 10.2$ – 10.4 .

Molecular docking and 3D-QSAR on 2-(oxalylamino) benzoic acid and its analogues as protein tyrosine phosphatase 1B inhibitors

pp 5521–5525

Mei Zhou and Mingjuan Ji*

The figure showed the inhibitor modification information derived from CoMFA model. Increasing bulk inside green regions and removing bulk from yellow regions favor the inhibitory activity; increasing negative charge in red regions and increasing positive charge in blue regions favor the inhibitory activity.



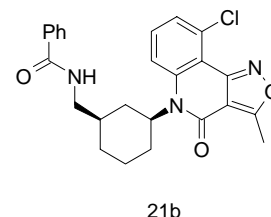
The contour plots of CoMFA steric fields (a) and electrostatic fields (b)

Cyclohexyl-linked tricyclic isoxazoles are potent and selective modulators of the multidrug resistance protein (MRP1)

pp 5526–5530

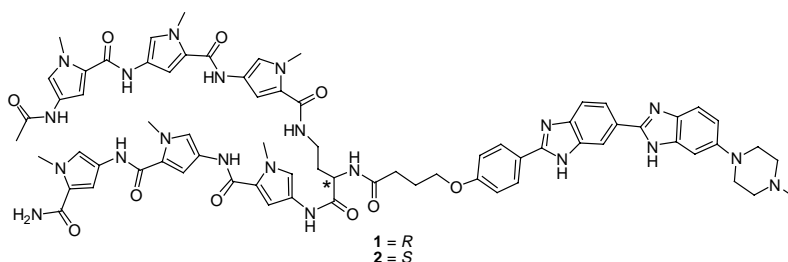
Bryan H. Norman,* Peter A. Lander, Joseph M. Gruber, Julian S. Kroin, Jeffrey D. Cohen, Louis N. Jungheim, James J. Starling, Kevin L. Law, Tracy D. Self, Linda B. Tabas, Daniel C. Williams, Donald C. Paul and Anne H. Dantzig

Novel cyclohexyl drug resistance modulators were synthesized and evaluated for in vitro inhibition of the drug resistance transporter, MRP1. This series resulted in the potent and selective MRP1 modulator **21b**, which demonstrated reversal of MRP1-mediated multidrug resistance in vivo.


Recognition of a 10 base pair sequence of DNA and stereochemical control of the binding affinity of chiral hairpin polyamide–Hoechst 33258 conjugates

pp 5531–5536

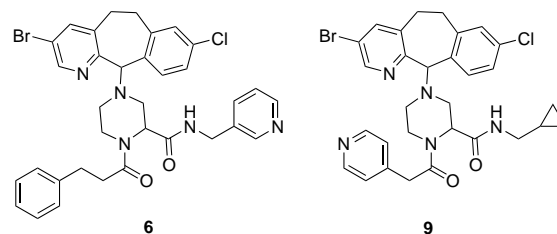
Putta Mallikarjuna Reddy, Joseph W. Toporowski, Alexandra L. Kahane and Thomas C. Bruice*


Surfing the piperazine core of tricyclic farnesyltransferase inhibitors

pp 5537–5543

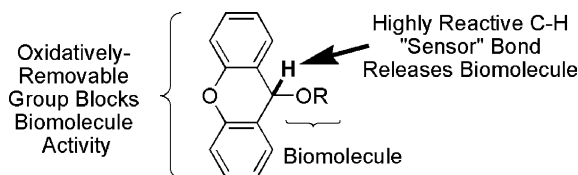
Laura L. Rokosz,* Chia-Yu Huang, John C. Reader, Tara M. Stauffer, Daniel Chelsky, Nolan H. Sigal, Ashit K. Ganguly and John J. Baldwin

An ECLiPS[®] library, containing 11,718 compounds, was used to explore the structure–activity relationships surrounding the piperazine core of tricyclic farnesyltransferase inhibitors. Compounds **6** and **9**, with IC₅₀S of less than 50 nM, are representative of the most potent structures identified from the screen.


An oxidatively releasable caging group that senses lipid peroxidation

pp 5544–5547

Kari A. Trumbull and Bruce P. Branchaud*

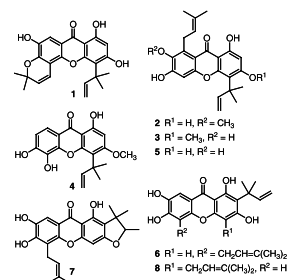


Antioxidant and cytotoxic activities of xanthenes from *Cudrania tricuspidata*

pp 5548–5552

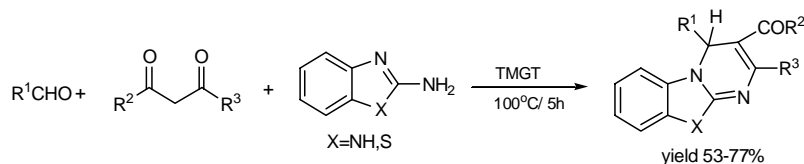
Byong Won Lee, Jin Hwan Lee, Sung-Tae Lee, Hyun Sun Lee, Woo Song Lee, Tae-Sook Jeong and Ki Hun Park*

The eight catecholic xanthenes with antioxidant and cytotoxic activities were isolated from *Cudrania tricuspidata*. Catecholic xanthenes possessed potent various free radical scavenging activities and also cytotoxicities against human cancer cell lines.

**A novel one-pot three-component reaction: Synthesis of triheterocyclic 4*H*-pyrimido[2,1-*b*]benzazoles ring systems**

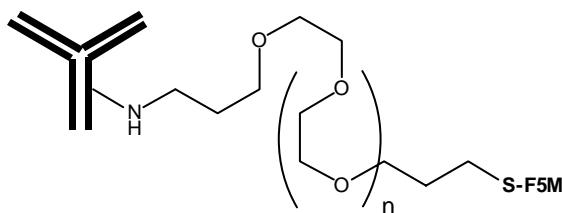
pp 5553–5557

Ahmad Shaabani,* Abbas Rahmati and Soheila Naderi

**An approach to heterobifunctional poly(ethyleneglycol) bioconjugates**

pp 5558–5561

Jane Li, Curtis F. Crasto, James S. Weinberg, Mansoor Amiji, Dinesh Shenoy, Srinivas Sridhar, Glenn J. Bubley and Graham B. Jones*

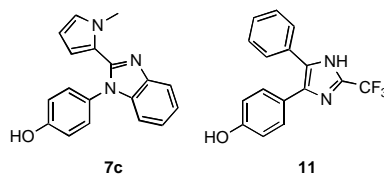


A series of differentially substituted PEG building has been assembled from a readily available precursor. Application is demonstrated in the form of PEG derivatized biomolecules including labeled antibody conjugates.

Estrogen receptor β selective ligands: Discovery and SAR of novel heterocyclic ligands

pp 5562–5566

Richard Chesworth,* Matthew D. Wessel, Lisa Heyden, F. Michael Mangano, Michael Zawistoski, Laura Gegnas, David Galluzzo, Bruce Lefker, Kimberly O. Cameron, Jeanne Tickner, Bihong Lu, Tessa A. Castleberry, Donna N. Petersen, Amy Brault, Pia Perry, Oicheng Ng, Thomas A. Owen, Lydia Pan, Hua-Zhu Ke, Thomas A. Brown, David D. Thompson and Paul DaSilva-Jardine



A series of ligands with varying heterocyclic cores and substituents that display a range of selectivities (up to >100 \times) for ER- β over ER- α are reported.

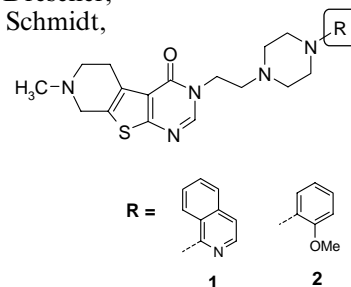


Synthesis and SAR of highly potent dual 5-HT_{1A} and 5-HT_{1B} antagonists as potential antidepressant drugs

pp 5567–5573

Andreas Kling,* Udo E. W. Lange, Helmut Mack, Margot H. M. Bakker, Karla U. Drescher, Wilfried Hornberger, Charles W. Hutchins, Achim Möller, Reinhold Müller, Martin Schmidt, Liliane Unger, Karsten Wicke, Kurt Schellhaas and Gerd Steiner

Novel 5-HT₁ autoreceptor ligands based on the tetrahydropyridothieno-pyrimidine core are described. Strategies for the development of dual antagonists for the 5-HT_{1A} and 5-HT_{1B} receptors based on **1** and **2** as leads are discussed. Compounds displaying high affinities and an antagonist mode of action were examined for selectivity and characterized in additional assays.

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i+ Supplementary data available via ScienceDirect

COVER

Amerliorating transthyretin amyloidogenesis by native state kinetic stabilization mediated by small molecule binding. Small molecule binding to the amyloidogenic protein transthyretin kinetically stabilizes the native tetrameric state, preventing dissociation to folded monomers that misfold and misassemble into toxic intermediates, amorphous aggregates, and amyloid fibrils. The Kelly laboratory has developed several structurally distinct inhibitor families, depicted in the background, that are undergoing pharmacological evaluation. Created by Steven M. Johnson, graduate student in Professor Jeffery W. Kelly's laboratory, Department of Chemistry, The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA.



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