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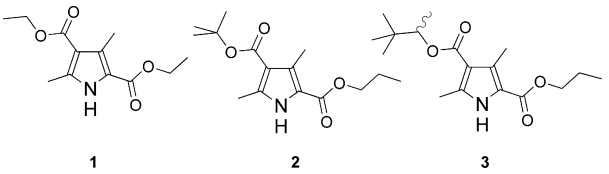
Synthesis and Pharmacological Characterisation of 2,4-Dicarboxy-pyrroles as Selective Non-Competitive mGluR1 Antagonists

Fabrizio Micheli,* Romano Di Fabio,* Paolo Cavanni, Joseph M. Rimland, Anna Maria Capelli, Cristiano Chiamulera, Mauro Corsi, Corrado Corti, Daniele Donati, Aldo Feriani, Francesco Ferraguti, Micaela Maffeis, Andrea Missio, Emiliangelo Ratti, Alfredo Paio, Roberta Pachera, Mauro Quartaroli, Angelo Reggiani, Fabio Maria Sabbatini, David G. Trist, Annarosa Ugolini and Giovanni Vitulli

GlaxoSmithkline Medicine Research Centre, Via Fleming, 4-37135 Verona, Italy



1 **2** **3**

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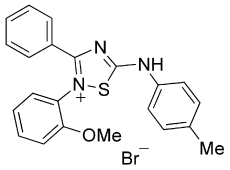
2,3-Diaryl-5-anilino[1,2,4]thiadiazoles as Melanocortin MC4 Receptor Agonists and Their Effects on Feeding Behavior in Rats

Kevin Pan, Malcolm K. Scott, Daniel H. S. Lee, Louis J. Fitzpatrick, Jeffery J. Crooke, Ralph A. Rivero, Daniel I. Rosenthal, Anil H. Vaidya, Boyu Zhao and Allen B. Reitz*

Drug Discovery Division, Johnson & Johnson Pharmaceutical Research and Development, Welsh and McKean Rds., PO Box 776, Spring House, PA 19477, USA

A new series of melanocortin (MC-4) receptor agonists was identified based upon high throughput screening of a corporate compound collection. Subsequent improvement of the activity led to compounds such as **3b** lowered food consumption in a fasting-induced feeding model in rats upon intraperitoneal administration.



3b, IC_{50} = 22 nM

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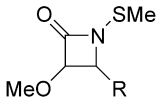
N-Thiolated β-Lactam Antibacterials: Defining the Role of Unsaturation in the C_4 Side Chain

Cristina Coates,[a] Timothy E. Long,[a] Edward Turos,[a,*] Sonja Dickey[b] and Daniel V. Lim[b]

[a]*Department of Chemistry, University of South Florida, Tampa, FL 33620, USA*
[b]*Department of Biology, University of South Florida, Tampa, FL 33620, USA*

This paper addresses the importance of unsaturation in the C_4 side chain R on antibacterial activity of *N*-methylthio β-lactams.



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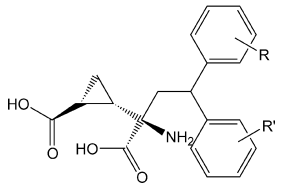
Synthesis and Structure–Activity Relationship Studies of Novel 2-Diarylethyl Substituted (2-Carboxycycloprop-1-yl)glycines as High-Affinity Group II Metabotropic Glutamate Receptor Ligands

Ulrik S. Sørensen, Thomas J. Bleisch, Anne E. Kingston, Rebecca A. Wright, Bryan G. Johnson, Darryle D. Schoepp and Paul L. Ornstein*

Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, DC 1523 Indianapolis, IN 46285, USA



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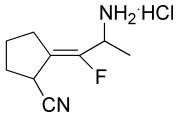
Inhibition of Dipeptidyl Peptidase IV (DPP IV) by 2-(2-Amino-1-fluoro-propylidene)-cyclopentanecarbonitrile, a Fluoroolefin Containing Peptidomimetic

Kake Zhao, Dong Sung Lim, Takashi Funaki and John T. Welch*

Department of Chemistry, University at Albany, Albany, NY 12222, USA



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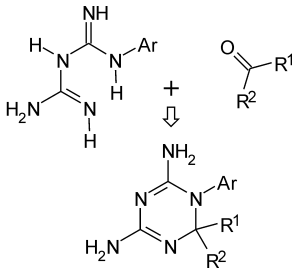
Synthesis of Solution-Phase Combinatorial Library of 4,6-Diamino-1,2-dihydro-1,3,5-triazine and Identification of New Leads Against A16V + S108T Mutant Dihydrofolate Reductase of *Plasmodium falciparum*

Tirayut Vilaivan,[a,*] Neungruthai Saesaengseerung,[a] Deanpen Jarprung,[b] Sumalee Kamchonwongpaisan,[b] Worachart Sirawaraporn[c] and Yongyuth Yuthavong[b]

[a]*Organic Synthesis Research Unit, Department of Chemistry, Faculty of Science, Chulalongkorn University, Phayathai Road, Patumwan, Bangkok 10330, Thailand*
[b]*National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Rama VI Road, Bangkok 10400, Thailand*
[c]*Department of Biochemistry, Faculty of Science, Mahidol University, Rama VI Road, Bangkok 10400, Thailand*

A 96-membered solution phase library of the titled compound was synthesized. Two highly potent inhibitors were identified by iterative deconvolution screening.



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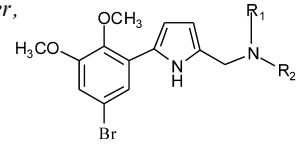
Synthesis of 2-(5-Bromo-2,3-dimethoxyphenyl)-5-(aminomethyl)-1*H*-pyrrole Analogues and Their Binding Affinities for Dopamine D_2, D_3, and D_4 Receptors

Robert H. Mach,[a,b,*] Yunsheng Huang,[a] Rebekah A. Freeman,[c] Li Wu,[a] Suwanna Blair[a] and Robert R. Luedtke[c]

[a]*Department of Radiology, PET Center, Wake Forest University School of Medicine, Winston-Salem, NC 27157, USA*
[b]*Department of Physiology and Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC 27157, USA*
[c]*Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, TX, 76107, USA*

The synthesis of a series of 2-(2,3-dimethoxyphenyl)-5-(aminomethyl)-1*H*-pyrrole analogues and their in vitro binding affinities for dopamine D_2, D_3, and D_4 receptors are presented.



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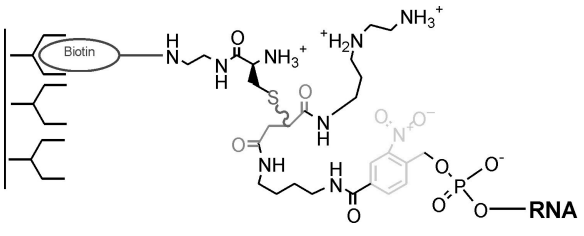
A Ribozyme with Michaelase Activity: Synthesis of the Substrate Precursors

Alexander Eisenführ,[a] Paramjit S. Arora,[b] Gerhard Sengle,[a] Leo R. Takaoka,[b] James S. Nowick[b] and Michael Famulok[a,*]

[a]*Kekulé-Institut für Organische Chemie und Biochemie, Rheinische Friedrich-Wilhelms-Universität Bonn, Gerhard-Domagk-Straße 1, 53121 Bonn, Germany*
[b]*Department of Chemistry, University of California, Irvine, Irvine, CA 92697-2025, USA*

The synthesis of the substrates and the substrate oligonucleotides used for the in vitro selection of a ribozyme that catalyzes a Michael reaction is described. We also describe the further characterization of this ribozyme with respect to substrate specificity.



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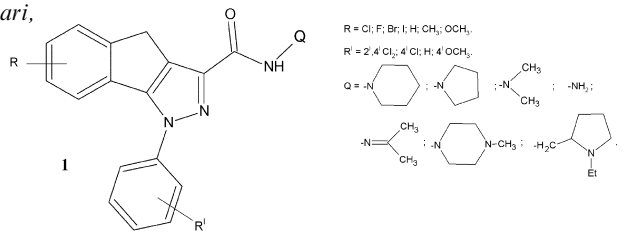
Tricyclic Pyrazoles. Part 1: Synthesis and Biological Evaluation of Novel 1,4-Dihydroindeno[1,2-*c*]pyrazol-Based Ligands for CB_1 and CB_2 Cannabinoid Receptors

Jean-Mario Mussinu,[a] Stefania Ruiu,[b] Antonio C. Mulè,[c] Amedeo Pau,[a] Mauro A. M. Carai,[b] Giovanni Loriga,[a,b] Gabriele Murineddu[a,b] and Gérard A. Pinna[a,*]

[a]*Dipartimento Farmaco Chimico Tossicologico, Università di Sassari, via F. Muroni 23/A, 07100 Sassari, Italy*
[b]*Neuroscienze S.c.a.r.l., Zona Industriale Macchiareddu, 09010 Uta, Cagliari, Italy*
[c]*Dipartimento di Scienze del Farmaco, Università di Sassari, via F. Muroni 23/A, 07100 Sassari, Italy*

Synthesis, CB_1 and CB_2 receptor affinities of 1,4-dihydroindeno [1,2-*c*]pyrazole carboxamides (**1**) are described



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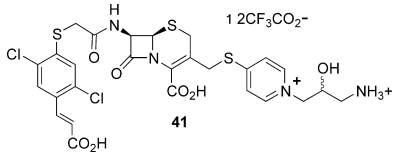
Anti-MRSA Cephems. Part 2: C-7 Cinnamic Acid Derivatives

Dane M. Springer,* Bing-Yu Luh, Jason T. Goodrich and Joanne J. Bronson

Anti-infective Chemistry, Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, PO Box 5100, Wallingford, CT 06492, USA

C-7 acidic cephems are described that have surprisingly good activity against methicillin-resistant *Staphylococcus aureus* (MRSA). The most active compound (**41**) displayed an MIC_{90} against MRSA of 1.0 μg/mL, and a PD_{50} of 0.8 mg/kg. A representative compound from this class was found to be very safe in a mouse model of acute toxicity.



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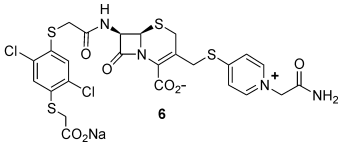
Anti-MRSA Cephems. Part 3: Additional C-7 Acid Derivatives

Dane M. Springer,* Bing-Yu Luh, Jason T. Goodrich and Joanne J. Bronson

Anti-infective Chemistry, Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, PO Box 5100, Wallingford, CT 06492, USA

Novel C-7 acid cephalosporin derivatives with good activity against methicillin-resistant *Staphylococcus aureus* (MRSA) are described. The most interesting compound (**6**) displayed an MIC_{90} against MRSA of 3.7 μg/mL, and an average PD_{50} of 3.9 mg/kg..



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New Minor Taxanes Analogues from the Needles of *Taxus Canadensis*

Qing Wen Shi,[a] Françoise Sauriol,[b] Orval Mamer[c] and Lolita O. Zamir[a,d,*]

[a]*Human Health Research Center, INRS-Institut Armand-Frappier, Universite du Quebec, 531 Boulevard des Prairies, Laval, Quebec, Canada H7V 1B7*
[b]*Department of Chemistry, Queen's University, Kingston, Ontario, Canada, K7L 3N6*
[c]*Biomedical Mass Spectrometry Unit, McGill University, 1130 Pine Avenue west, Montreal, Quebec, Canada, H3A 1A3*
[d]*McGill Centre for Translational Research in Cancer, Sir Mortimer B. Davis-Jewish General Hospital, 3755 Cote Ste.Catherine Rd. Suite D-127, Montreal, Quebec, Canada H3T 1E2*

New taxanes with different conformations of the core skeleton were isolated from the needles of the Canadian yew. Their lack of activity towards tubulin assembly is discussed.