Graphical Abstracts

Bioorg. Med. Chem. 11 (2003) 4303

Design, Synthesis, and Anticancer Activity of Phosphonic Acid Diphosphate Derivative of Adenine-Containing Butenolide and Its Water-Soluble Derivatives of Paclitaxel with High Antitumor Activity

Ali A. Moosavi-Movahedi,[a,*] Shahram Hakimelahi,[b] Jamshid Chamani,[a] Ghadam Ali Khodarahmi,[c] Farshid Hassanzadeh,[c] Fen-Tair Luo,[d] Tai Wei Ly,[d] Kak-Shan Shia,[e] Chi-Feng Yen,[e] Moti L. Jain,[f] Ramasamy Kulatheeswaran,[d] Cuihua Xue,[d] Manijeh Pasdar[b] and Gholam Hossein Hakimelahi[a,d,e,*]

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[b]*Department of Cell Biology, Faculty of Medicine, University of Alberta, Edmonton, Alberta, Canada, T6G 2H7*
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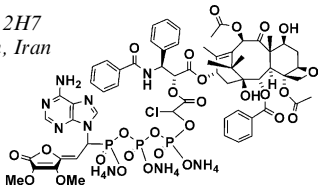

Bioorg. Med. Chem. 11 (2003) 4315

The Discovery of BMS-275183: An Orally Efficacious Novel Taxane

Harold Mastalerz,[a,*] Donald Cook,[a] Craig R. Fairchild,[b] Steven Hansel,[c] Walter Johnson,[a] John F. Kadow,[a] Byron H. Long,[b] William C. Rose,[b] James Tarrant,[a] Mu-Jen Wu,[a] May Quifen Xue,[a] Guifen Zhang,[a] Mary Zoeckler[c] and Dolatrai M. Vyas[a]

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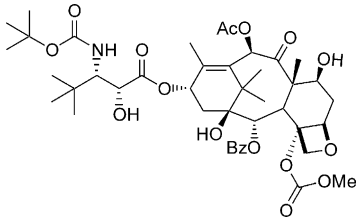

Bioorg. Med. Chem. 11 (2003) 4325

Synthesis of a High-Affinity Fluorescent PPARγ Ligand for High-Throughput Fluorescence Polarization Assays

Michael J. DeGrazia,[a] Jerry Thompson,[b] John P. Vanden Heuvel[b] and Blake R. Peterson[a,*]

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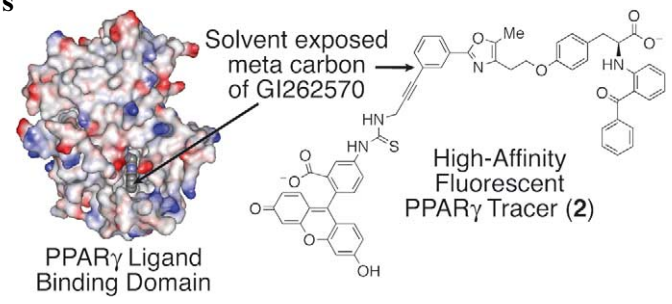
[b]*Department of Veterinary Sciences and Center for Molecular Toxicology, The Pennsylvania State University, University Park, PA 16802, USA*

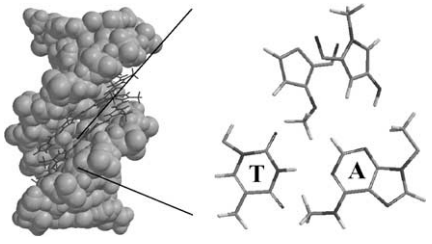


Bioorg. Med. Chem. 11 (2003) 4333

Shape Selective Recognition of T·A Base Pairs by Hairpin Polyamides Containing N-Terminal 3-Methoxy (and 3-Chloro) Thiophene Residues

Shane Foister, Michael A. Marques, Raymond M. Doss and Peter B. Dervan*

The Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125, USA



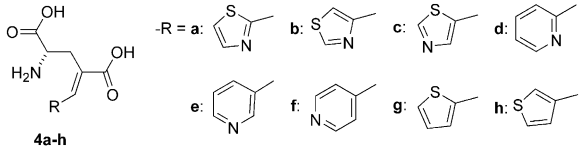
Bioorg. Med. Chem. 11 (2003) 4341

Synthesis and In Vitro Pharmacology at AMPA and Kainate Preferring Glutamate Receptors of 4-Heteroarylmethylidene Glutamate Analogues

Jon Valgeirsson,[a] Jeppe K. Christensen,[c] Anders S. Kristensen,[b] Darryl S. Pickering,[b] Birgitte Nielsen,[a] Christina H. Fischer,[a] Hans Bräuner-Osborne,[a] Elsebet Ø. Nielsen,[c] Povl Krogsgaard-Larsen[a] and Ulf Madsen[a,*]

[a]*Department of Medicinal Chemistry, The Danish University of Pharmaceutical Sciences, 2 Universitetsparken, DK-2100 Copenhagen, Denmark*
[b]*Department of Pharmacology, The Danish University of Pharmaceutical Sciences, 2 Universitetsparken, DK-2100 Copenhagen, Denmark*
[c]*NeuroSearch A/S, 93 Pederstrupvej, DK-2750 Ballerup, Denmark*

Compound **4a** was shown to be a potent GluR5 agonist with lower affinities towards the AMPA receptor subtypes GluR1–4.



Bioorg. Med. Chem. 11 (2003) 4351

Synthesis and In Vitro Antitumor Activity of an Isomer of the Marine Pyridoacridine Alkaloid Ascididemin and Related Compounds

Evelyne Delfourne,[a,*] Robert Kiss,[b] Laurent Le Corre,[a] Joumaa Merza,[a] Jean Bastide,[a] Armand Frydman[c] and Francis Darro[c]

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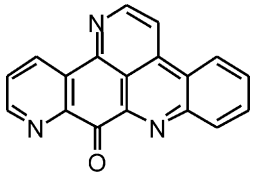
[b]*Laboratoire d'Histopathologie, Faculté de Médecine, Université Libre de Bruxelles, 808 Route de Lennik, 1070 Bruxelles, Belgium*
[c]*Cephalon France, Centre de Recherches, 19 avenue du Pr Cadiot, BP 22, 94701 Maisons-Alfort Cedex, France*



Bioorg. Med. Chem. 11 (2003) 4357

Antiprotozoal Activities of Symmetrical Bishydroxamic Acids

Duy H. Hua,[a,*] Masafumi Tamura,[a] Masahiro Egi,[a] Karl Werbovetz,[b] Dawn Delfín,[b] Manar Salem[b] and Peter K. Chiang[c]

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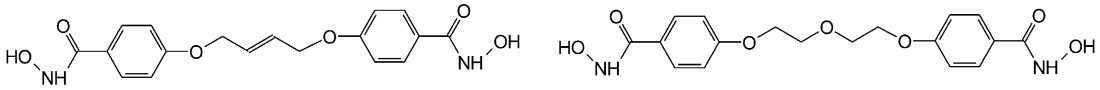
[b]*Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, 500 West 12th Avenue, Columbus, OH 43210, USA*
[c]*Department of Applied Biochemistry, Walter Reed Army Institute of Research, Washington, DC 20307-5100, USA*



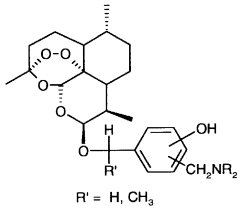
Bioorg. Med. Chem. 11 (2003) 4363

Artemisinin Derivatives Bearing Mannich Base Group: Synthesis and Antimalarial Activity

Ying Li,[a,*] Zhong-Shun Yang,[a] Hong Zhang,[a] Ben-Jun Cao,[a] Fang-Dao Wang,[a] Yu Zhang,[a] Yun-Lin Shi,[b] Jun-De Yang[b] and Bo-An Wu[b]

[a]*Department of Synthetic Chemistry, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 201203, China*
[b]*Department of Malaria, Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences, Beijing 100071, China*

A new type of artemisinin derivatives bearing Mannich base group was prepared and compared with artesunate in mice infected with *P. berghei*. Two most potent derivatives **17b** and **17d** were further examined for antimalarial activity against *P. knowlesi* in rhesus monkeys.



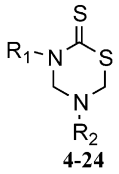
Bioorg. Med. Chem. 11 (2003) 4369

Synthesis and Antimycobacterial Activity of 3,5-Disubstituted Thiadiazine Thiones

D. Katiyar,[a] V.K. Tiwari,[a] R.P. Tripathi,[a,*] A. Srivastava,[b] V. Chaturvedi,[b] R. Srivastava[b] and B.S. Srivastava[b]

[a]*Division of Medicinal Chemistry, Central Drug Research Institute, Lucknow-226001, India*
[b]*Division of Microbiology, Central Drug Research Institute, Lucknow-226001, India*

A series of thiadiazine thiones **4**–**24** were synthesised and evaluated for antitubercular activity. One of the compounds showed in vitro (against MDR *Mycobacterium tuberculosis* H37Rv strains) and in vivo activity.



4-24

Bioorg. Med. Chem. 11 (2003) 4377

Optically Active 2-Benzyl-3-methanesulfinylpropanoic Acid: Synthesis and Evaluation as Inhibitors for Carboxypeptidase A

Jing-Yi Jin,[a] Guan Rong Tian[a] and Dong H. Kim[b,*]

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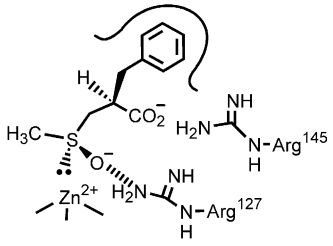
[b]*Center for Integrated Molecular Systems, Division of Molecular and Life Sciences, Pohang University of Science and Technology, San 31Hyoja-dong, Namku, Pohang 790-784, South Korea*

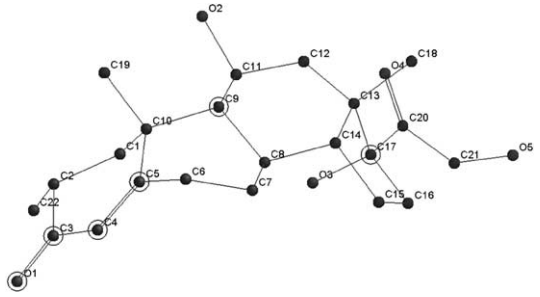


Bioorg. Med. Chem. 11 (2003) 4383

Study of the Binding Affinity for Corticosteroid-Binding Globulin (CBG) Using the Electron Topological Method (ETM) as Three-Dimensional Quantitative Structure–Activity Relationship (3D QSAR)

Yahya Guzel* and Emel Ozturk

Erciyes University, Faculty of Science and Art, Departments of Chemistry, 38039 Kayseri, Turkey



Bioorg. Med. Chem. 11 (2003) 4389

A Conformational Restriction Approach to the Development of Dual Inhibitors of Acetylcholinesterase and Serotonin Transporter as Potential Agents for Alzheimer's Disease

Narihiro Toda,[a] Keiko Tago,[a] Shinji Marumoto,[a] Kazuko Takami,[a] Mayuko Ori,[a] Naho Yamada,[a] Kazuo Koyama,[b] Shunji Naruto,[b] Kazumi Abe,[c] Reina Yamazaki,[c] Takao Hara,[c] Atsushi Aoyagi,[c] Yasuyuki Abe,[c] Tsugio Kaneko[c] and Hiroshi Kogen[a,*]

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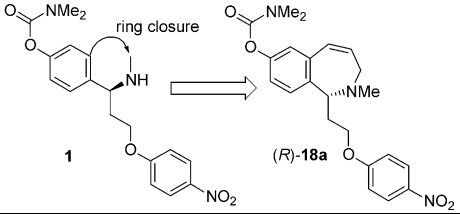

Bioorg. Med. Chem. 11 (2003) 4417

Synthesis of Totarol Amino Alcohol Derivatives and Their Antiplasmodial Activity and Cytotoxicity

Cailean Clarkson,[a] Chitalu C. Musonda,[b] Kelly Chibale,[b,*] William E. Campbell[a] and Peter Smith[a]

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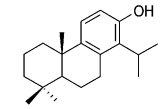
[b]*Department of Chemistry, University of Cape Town, Private Bag, Rondebosch 7701, South Africa*

A novel series of β-amino alcohols (**7**–**13**) were synthesised from totarol (**3**) and screened for in vitro antiplasmodial activity and cytotoxicity. These compounds showed IC_{50} values in the range of 0.6–3.0 μM against drug resistant and sensitive strains of *Plasmodium falciparum*, while exhibiting little cytotoxicity against a mammalian cell line.



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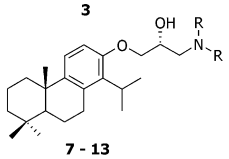

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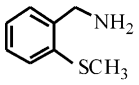
Bioorg. Med. Chem. 11 (2003) 4423

Inactivation of Mitochondrial Monoamine Oxidase B by Methylthio-Substituted Benzylamines

Xingliang Lu, María Rodríguez, Wenxin Gu and Richard B. Silverman*

Department of Chemistry, Department of Biochemistry, Molecular Biology, and Cell Biology, and the Drug Discovery Program, Northwestern University, Evanston, IL 60208-3113, USA



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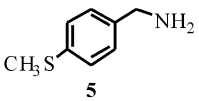

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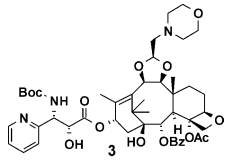
Bioorg. Med. Chem. 11 (2003) 4431

New Highly Active Taxoids from 9β-Dihydrobaccatin-9,10-acetals. Part 4

Yasuyuki Takeda,[a] Kouichi Uoto,[a] Jun Chiba,[a] Takao Horiuchi,[a] Michio Iwahana,[b] Ryo Atsumi,[c] Chiho Ono,[c] Hirofumi Terasawa[b] and Tsunehiko Soga[a,*]

[a]*Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co., Ltd., Tokyo R&D Center, 16-13 Kita-Kasai 1-Chome, Edogawa-ku, Tokyo 134-8630, Japan*
[b]*New Product Research Laboratories III, Daiichi Pharmaceutical Co., Ltd., Tokyo R&D Center, 16-13 Kita-Kasai 1-Chome, Edogawa-ku, Tokyo 134-8630, Japan*
[c]*Drug Metabolism & Physicochemical Property Research Laboratory, Daiichi Pharmaceutical Co., Ltd., Tokyo R&D Center, 16-13 Kita-Kasai 1-Chome, Edogawa-ku, Tokyo 134-8630, Japan*

It was shown that a new taxane analogue (**3**) was prone to be metabolized by human liver microsomes. We identified a major metabolite, M-1, and to improve the metabolic stability of **3**, new taxane analogues were synthesized. Some compounds maintained antitumor activity and were scarcely metabolized by human liver microsomes.



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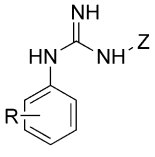
Bioorg. Med. Chem. 11 (2003) 4449

Arylguanidine and Arylbiguanide Binding at 5-HT_3 Serotonin Receptors: A QSAR Study

Richard A. Glennon,[a,*] Maha Khalifa Daoud,[a] Małgorzata Dukat,[a] Milt Teitler,[b] Katharine Herrick-Davis,[b] Anil Purohit[b] and Hasan Syed[b]

[a]*Department of Medicinal Chemistry, School of Pharmacy, Virginia Commonwealth University, Richmond VA 23298, USA*
[b]*Center for Neuropharmacology and Neuroscience, Albany Medical College, Albany, NY 12208, USA*

A QSAR investigation for 5-HT_3 binding reveals that the affinity of arylguanidines (Z = H) and arylbiguanides [Z = C(NH)NH_2] is influenced by electronic, lipophilic, and other descriptors. In particular, molecular polarizability, a Chi index, and E-state values provide significant correlations.

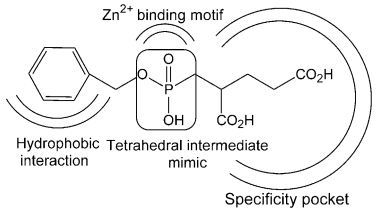


Bioorg. Med. Chem. 11 (2003) 4455

Conformational and SAR Analysis of NAALADase and PSMA Inhibitors

A. Jayne Oliver,[a] Olaf Wiest,[a,*] Paul Helquist,[a] Marvin J. Miller[a] and Martin Tenniswood[b]

[a]*Walther Cancer Research Center, Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame IN 46556-5670, USA*
[b]*Department of Biological Sciences, University of Notre Dame, Notre Dame IN 46556-5670, USA*



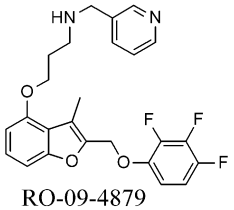
Bioorg. Med. Chem. 11 (2003) 4463

Synthesis and Biological Activities of Benzofuran Antifungal Agents Targeting Fungal *N*-Myristoyltransferase

Miyako Masubuchi, Hirosato Ebiike, Ken-ichi Kawasaki, Satoshi Sogabe, Kenji Morikami, Yasuhiko Shiratori, Shinji Tsujii, Toshihiko Fujii, Kiyoaki Sakata, Michiko Hayase, Hidetoshi Shindoh, Yuko Aoki, Tatsuo Ohtsuka* and Nobuo Shimma

Chugai Pharmaceutical Kamakura Research Center (formerly Nippon Roche Research Center), 200 Kajiwara, Kamakura, Kanagawa 247-8530, Japan

The C-4 side-chain modification of lead compound **1** has resulted in the identification of a potent and selective *Candida albicans N*-myristoyltransferase (CaNmt) inhibitor RO-09-4609. Further modification of its C-2 substituent has led to the discovery of RO-09-4879, which exhibits antifungal activity in vivo. The optimization incorporates various biological investigations including a quasi in vivo assay and pharmacokinetic study. The computer aided drug design, synthesis, structure–activity relationships and biological properties of RO-09-4879 are described in detail.

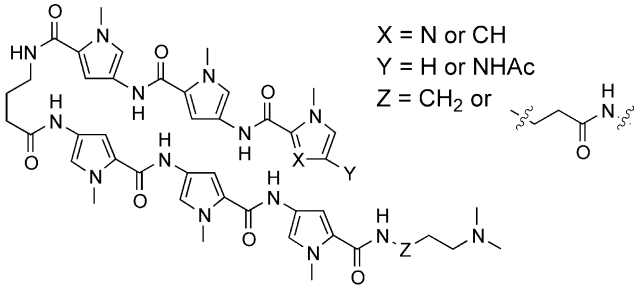


Bioorg. Med. Chem. 11 (2003) 4479

Comprehensive High-Resolution Analysis of Hairpin Polyamides Utilizing a Fluorescent Intercalator Displacement (FID) Assay

Winston C. Tse, Takahiro Ishii and Dale L. Boger*

Department of Chemistry and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA

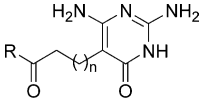


Bioorg. Med. Chem. 11 (2003) 4487

Design, Synthesis, and Biological Evaluation of Simplified α-Keto Heterocycle, Trifluoromethyl Ketone, and Formyl Substituted Folate Analogues as Potential Inhibitors of GAR Transformylase and AICAR Transformylase

Thomas H. Marsilje,[a,c] Michael P. Hedrick,[a,c] Joel Desharnais,[a,c] Ali Tavassoli,[d] Yan Zhang,[b,c] Ian A. Wilson,[b,c] Stephen J. Benkovic[d] and Dale L. Boger[a,c,*]

[a]*Department of Chemistry, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*
[b]*Department of Molecular Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*
[c]*The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*
[d]*Department of Chemistry, Pennsylvania State University, University Park, PA 16802, USA*



A novel series of potential inhibitors of glycinamide ribonucleotide transformylase (GAR Tfase) and aminoimidazole carboxamide transformylase (AICAR Tfase) that incorporate an electrophilic carbonyl group is reported.

Bioorg. Med. Chem. 11 (2003) 4503

10-(2-Benzoxazolcarbonyl)-5,10-dideaza-acyclic-5,6,7,8-tetrahydrofolic Acid: A Potential Inhibitor of GAR Transformylase and AICAR Transformylase

Thomas H. Marsilje,[a,c] Michael P. Hedrick,[a,c] Joel Desharnais,[a,c] Kevin Capps,[a,c] Ali Tavassoli,[d] Yan Zhang,[b,c] Ian A. Wilson,[b,c] Stephen J. Benkovic[d] and Dale L. Boger[a,c,*]

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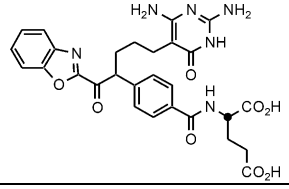
[b]*Department of Molecular Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*
[c]*The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*
[d]*Department of Chemistry, Pennsylvania State University, University Park, PA 16802, USA*



The design and synthesis of 10-(2-benzoxazolcarbonyl)-DDACTHF as an inhibitor of glycinamide ribonucleotide transformylase (GAR Tfase) and aminoimidazole carboxamide transformylase (AICAR Tfase) are reported.

Bioorg. Med. Chem. 11 (2003) 4511

Design, Synthesis and Biological Evaluation of 10-CF_3CO-DDACTHF Analogues and Derivatives as Inhibitors of GAR Tfase and the De Novo Purine Biosynthetic Pathway

Joel Desharnais,[a,c] Inkyu Hwang,[a,c] Yan Zhang,[b,c] Ali Tavassoli,[d] Justin Baboval,[d] Stephen J. Benkovic,[d] Ian A. Wilson[b,c] and Dale L. Boger[a,c,*]

[a]*Department of Chemistry, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*
[b]*Department of Molecular Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*
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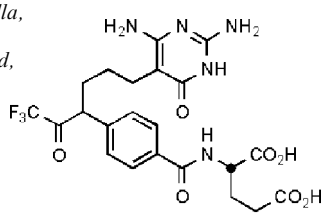

The synthesis and evaluation of analogues and key derivatives of 10-CF_3CO-DDACTHF (**1**) as inhibitors of glycinamide ribonucleotide transformylase (GAR Tfase) and aminoimidazole carboxamide transformylase (AICAR Tfase) are reported.

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QSAR Study on Tadpole Narcosis

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This paper deals with a Quantitative Structure–Activity Relationship (QSAR) study on a large set of 123 compounds using a combination of topological indices as well as Abraham's molecular descriptors. The results have shown that an excellent model ($R = 0.9542$) is obtained in hexa-parametric correlation containing W, logRB (topological indices) along with R_2, $\Sigma\pi_2^H$, $\Sigma\beta_2^O$ and V_x as the correlating parameters. The results are discussed critically.