Graphical Abstracts

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Enoyl-CoA Hydratase: Reaction, Mechanism, and Inhibition

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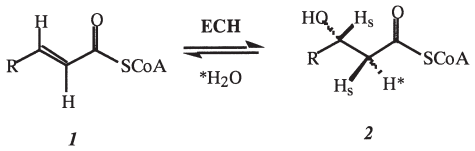
This review summarizes the current knowledge of the reaction, mechanism and inhibition of enoyl-CoA hydratase which catalyzes the interconvertion of **1** and **2**, the 2nd step in the β-oxidation pathway of fatty acid metabolism.



1 *2*

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Crystal Structures of Reversible Ketone-Based Inhibitors of the Cysteine Protease Cruzain

Lily Huang,[a] Linda S. Brinen[b,*] and Jonathan A. Ellman[a,*]

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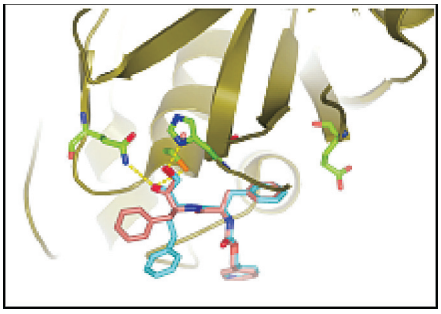
[b]*Department of Pathology, University of California, San Francisco, CA 94143, USA*

The crystal structures of two hydroxymethyl ketone inhibitors complexed to the cysteine protease cruzain have been determined at 1.1 and 1.2 Å resolution, respectively. These high resolution crystal structures provide the first structures of non-covalent inhibitors bound to cruzain. A series of compounds were prepared and tested based upon the structures providing further insight into the key binding interactions.



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N-(Trifluoromethyl)benzyl Substituted *N*-Normetazocines and *N*-Norketobemidones

Everette L. May,[a] Andrew Coop,[b,*] James H. Woods,[c] Mario D. Aceto,[a] Edward R. Bowman,[a] Louis S. Harris[a] and John R. Traynor[c]

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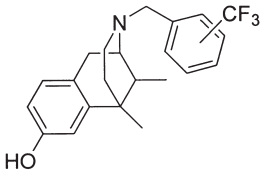
[b]*Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, 20 North Pine Street, Baltimore, MD 21201, USA*
[c]*Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48109, USA*



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Synthesis and Antibacterial Activity of 5-Substituted Oxazolidinones

O. A. Phillips,[a,*] E. E. Udo,[b] A. A. M. Ali[c] and N. Al-Hassawi[a]

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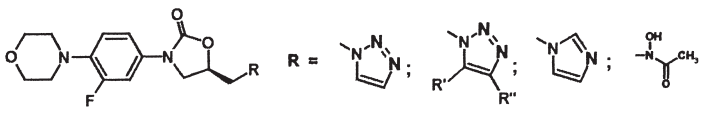
[c]*Department of Chemistry, Faculty of Science, Kuwait University, PO Box 5969, Safat 13060, Kuwait*



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Structure-Based Mutagenesis Approaches Toward Expanding the Substrate Specificity of D-2-Deoxyribose-5-phosphate Aldolase

Grace DeSantis,[a] Junjie Liu,[a] David P. Clark,[b] Andreas Heine,[c] Ian A. Wilson[c] and Chi-Huey Wong[a,*]

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[b]*Department of Microbiology, University of Illinois, Urbana, IL 61801, USA*
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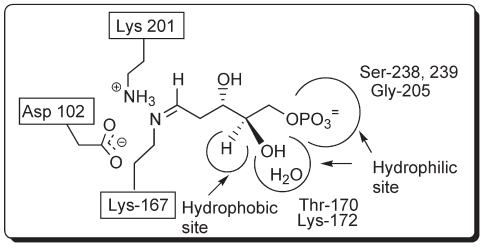

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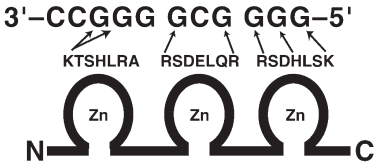
GFP-Linked Zinc Finger Protein Sp1: Fluorescence Study and Implication for N-Terminal Zinc Finger 1 as Hinge Finger

Keizo Matsushita and Yukio Sugiura

Institute for Chemical Research, Kyoto University, Uji, Kyoto 611-0011, Japan

The detail information of the N-terminal size finger of Sp1 has been described.



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Synthesis of New 2,4-Diaminopyrido[2,3-*d*]pyrimidine and 2,4-Diaminopyrrolo[2,3-*d*]pyrimidine Inhibitors of *Pneumocystis carinii*, *Toxoplasma gondii*, and *Mycobacterium avium* Dihydrofolate Reductase

Andre Rosowsky,[a,*] Han Chen,[a] Hongning Fu[a] and Sherry F. Queener[b]

[a]*Dana-Farber Cancer Institute and Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115, USA*
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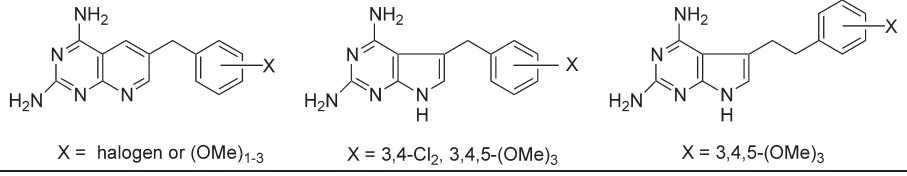

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^{19}F NMR Studies of Tryptophan/Serum Albumin Binding

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Using D- and L-6-fluorotryptophan as probes, ^{19}F NMR provides direct measures of the Trp binding avidity of 'fatty acid free' bovine serum albumin. Both a high and low affinity binding site are present. In the case of L-6-fluorotryptophan separate signals are observed for the high and low affinity binding sites and titrations with competing ligands can be used to establish the relative affinities of ligands. Binding at the high affinity site appears to be hydrophobic and shape specific with L-Phe being a very poor ligand (KD[L-Phe]/ KD[L-Trp] = 800) while naphthylalanine containing peptides displace L-6-fluorotryptophan from this site. Octanoic acid addition disrupts binding at both sites. This NMR assay appears well-suited for the discovery of selective binding agents in this and other biorecognition phenomena.

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Quinazolines as Adenosine Receptor Antagonists: SAR and Selectivity for A_{2B} Receptors

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[b]*Molecular Recognition Section, Laboratory of Bioorganic Chemistry, NIDDK, NIH, Bldg. 8A, Rm. B1A 17, Bethesda, MD 20892-0810, USA*
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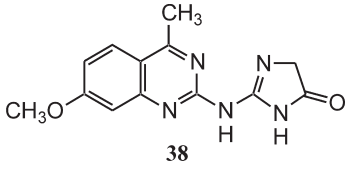
We have recently reported the discovery of numerous new compounds that are selective inhibitors of all of the subtypes of the adenosine receptor family via a pharmacophore database searching and screening strategy. During the course of this work we made the unexpected discovery of a potent A_{2B} receptor antagonist, 4-methyl-7-methoxyquinazolyl-2-(2′-amino-4′-imidazolinone) (**38**, CMB 6446), which showed selectivity for this receptor and functioned as an antagonist, with a binding K_i value of 112 nM. We explored the effects of both substituent- and ring-structural variations on the receptor affinity in this series of derivatives, which were found to be mostly non-selective adenosine receptor ligands with K_i values in the micromolar range. Since no enhancement of A_{2B} receptor affinity of **38** was achieved, the previously reported pharmacophore-based searching strategy yielded the most potent and selective structurally-related hit in the database originally searched.



38

K_i (A_{2B}) = 112 nM

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Solid-Phase Synthesis of Diamine and Polyamine Amino Acid Derivatives as HIV-1 Tat-TAR Binding Inhibitors

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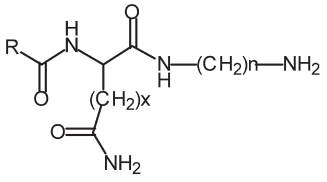
A series of diamine and polyamine derivatives of aspartic and glutamic acid were prepared using Rink Amide solid phase synthesis. The derivatives were all evaluated for their ability to inhibit Tat–TAR binding using a FIGS cellular assay.



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Three-Dimensional Pharmacophore Hypotheses of Octopamine/ Tyramine Agonists which Inhibit [1-^{14}C]Acetate Incorporation in *Plodia interpunctella*

Akinori Hirashima,[a] Tomohiko Eiraku,[b] Yoko Shigeta[c] and Eiichi Kuwano[a]

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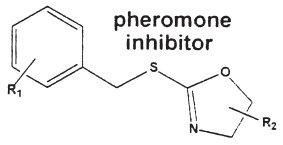
[c]*Department of Bioresource and Bioenvironmental Sciences, School of Agriculture, Kyushu University, Fukuoka 812-8581, Japan*

Three-dimensional pharmacophore hypotheses were built from a set of 36 octopamine (OA)/ tyramine (TA) agonists responsible for the inhibition of sex-pheromone production in *Plodia interpunctella*. Among the ten chemical-featured models generated by a program Catalyst/Hypo, hypotheses including hydrogen-bond acceptor (HBA), hydrogen-bond acceptor aliphatic (HBAl), hydrophobic (Hp), hydrophobic aromatic (HpAr) and hydrophobic aliphatic (HpAl) features were considered to be important and predictive in evaluating OA/TA agonists.



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Structure–Activity Relationship Studies on Chalcone Derivatives: The Potent Inhibition of Chemical Mediators Release

Horng-Huey Ko,[a] Lo-Ti Tsao,[b] Kun-Lung Yu,[c] Cheng-Tsung Liu,[c] Jih-Pyang Wang[b] and Chun-Nan Lin[c,*]

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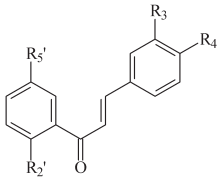
[c]*School of pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan 807, Republic of China*

A series of chalcone derivative have been synthesized and the anti-inflammatory effect was described.



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N-, α-, and β-Substituted 3-Aminopropionic Acids: Design, Syntheses and Antiseizure Activities

C.Y.K. Tan,[a] D. Wainman[a] and D.F. Weaver[a,b]

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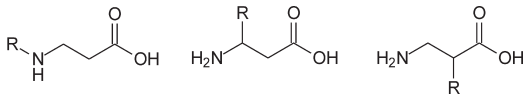
[b]*Departments of Neurology and Chemistry, Dalhousie University, Halifax, Nova Scotia, Canada, B3H 4J3*



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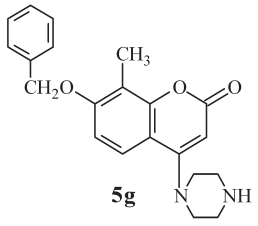
Coumarin, Chromone, and 4(3*H*)-pyrimidinone Novel Bicyclic and Tricyclic Derivatives as Antiplatelet Agents: Synthesis, Biological Evaluation, and Comparative Molecular Field Analysis

Giorgio Roma,[a,*] Mario Di Braccio,[a] Antonio Carrieri,[b] Giancarlo Grossi,[a] Giuliana Leoncini,[c] Maria Grazia Signorello[c] and Angelo Carotti[b,*]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Genova, viale Benedetto XV, 16132 Genoa, Italy*
[b]*Dipartimento Farmacochimico, Università di Bari, via Orabona 4, 70125 Bari, Italy*
[c]*Dipartimento di Medicina Sperimentale, Sezione Biochimica, Università di Genova, viale Benedetto XV, 16132 Genoa, Italy*

Several title compounds were synthesized and evaluated in vitro for their inhibitory properties on human platelet aggregation. Among them, the substituted 4-(1-piperazinyl)coumarin **5g** displayed the highest activity: IC_{50} (μM) 1.9±0.2 (ADP, 5.0 μM), 1.8±0.4 (collagen, 5.0 μg/mL), 1.1±0.2 (A23187, 20.0 μM). Structure–antiplatelet activity relationship studies of the previously and now described compounds led to the development of a statistically robust CoMFA model showing at the 3-D level the main interactions modulating the biological activity.



5g

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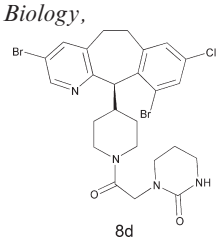
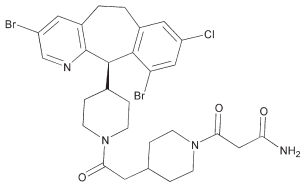
Trihalobenzocycloheptapyridine Analogues of Sch 66336 as Potent Inhibitors of Farnesyl Protein Transferase

F. George Njoroge,* Bancha Vibulbhan, Patrick Pinto, Corey L. Strickland, W. Robert Bishop, Paul Kirschmeir, V. Girijavallabhan and Ashit K. Ganguly

Schering-Plough Research Institute, Departments of Chemistry and Tumor Biology, 2015 Galloping Hill Road, Kenilworth, NJ 07033, USA



8d



4c

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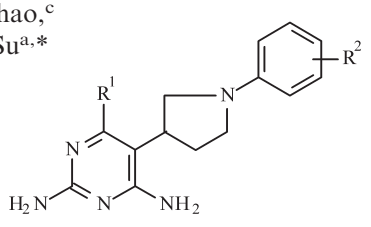
Non-classical Antifolates, 5-(*N*-Phenylpyrrolidin-3-yl)-2,4,6-triaminopyrimidines and 2,4-Diamino-6(5*H*)-oxopyrimidines, Synthesis and Antitumor Studies

Yen-Lin Huang,[a,b] Chyun-Feng Lin,[a,b] Yi-Jen Lee,[a] Wei-Wei Li,[c] Ting-Chou Chao,[c] Valeriy A. Bacherikov,[a] Kuo-Tung Chen,[b] Chin-Ming Chen[b] and Tsann-Long Su[a,*]

[a]*Laboratory of Bioorganic Chemistry, Institute of Biomedical Sciences, Academia Sinica, Taipei 115, Taiwan*
[b]*Department of Medicinal Chemistry, College of Pharmacy, Taipei Medical University, Taipei, Taiwan*
[c]*Molecular Pharmacology and Therapeutics Program, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA*

A series of non-folate analogues was synthesized and their SAR were studied.



R_1 = NH_2, OH
R_2 = H, OMe, NO_2, CN, F, Cl, Br

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Carbohydrate-Centered Maleimide Cluster as a New Type of Templates for Multivalent Peptide Assembling: Synthesis of Multivalent HIV-1 gp41 Peptides

Lai-Xi Wang, Jiahong Ni and Suddham Singh

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