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Bioorganic & Medicinal Chemistry

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Bioorganic & Medicinal Chemistry Vol. 17, No. 7, 2009

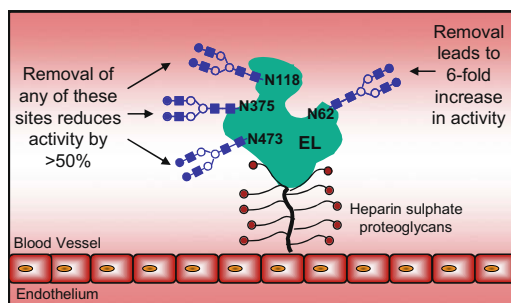
Contents

REVIEW

The effect of individual N-glycans on enzyme activity

pp 2645–2653

Danielle Skropeta*



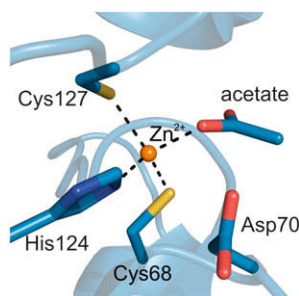
A review featuring 142 citations covering the recent literature on the modulation of enzyme function by N-linked glycosylation.

ARTICLES

Carbonic anhydrase inhibitors. Inhibition of the β -class enzymes from the fungal pathogens *Candida albicans* and *Cryptococcus neoformans* with aliphatic and aromatic carboxylates

pp 2654–2657

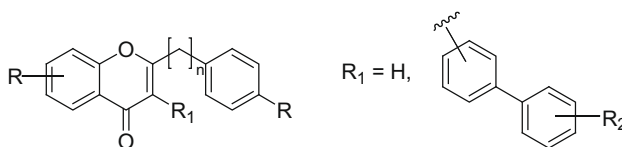
Alessio Innocenti, Rebecca A. Hall, Christine Schlicker, Fritz A. Mühlischlegel, Claudiu T. Supuran*



Synthesis, activity and molecular modeling of a new series of chromones as low molecular weight protein tyrosine phosphatase inhibitors

pp 2658–2672

Marco Forghieri, Christian Laggner, Paolo Paoli, Thierry Langer, Giampaolo Manao, Guido Camici, Lucia Bondioli, Fabio Prati, Luca Costantino*



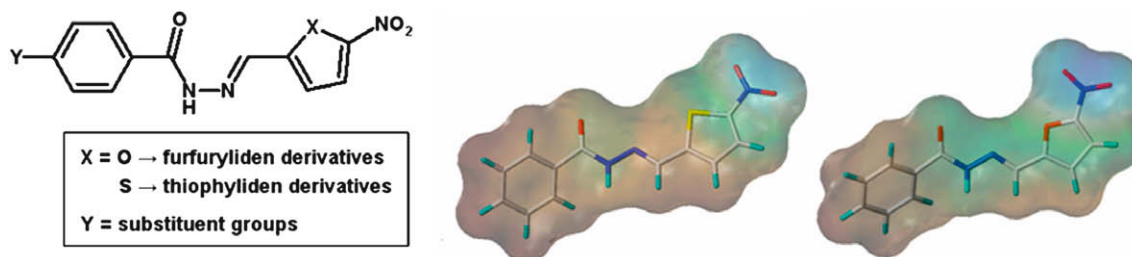
A series of chromones has been discovered as low molecular weight protein tyrosine phosphatase inhibitors, active in vitro and on cells, potentially useful for the treatment of cancer and Type II diabetes. These compounds inhibit also PTP-1B. Molecular modeling studies suggest the binding mode of these compounds to the enzyme.



Molecular modeling studies and in vitro bioactivity evaluation of a set of novel 5-nitro-heterocyclic derivatives as anti-*T. cruzi* agents

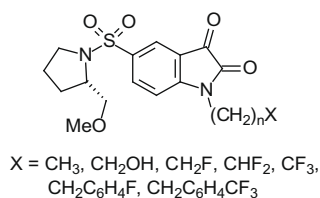
pp 2673–2679

Fávero Reisdorfer Paula, Salomão Dória Jorge, Leonardo Viana de Almeida, Kerly Fernanda Mesquita Pasqualoto, Leoberto Costa Tavares*


Fluorinated isatin derivatives. Part 1: Synthesis of new N-substituted (S)-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatins as potent caspase-3 and -7 inhibitors

pp 2680–2688

Anil Kumar Podichetty, Andreas Faust, Klaus Kopka, Stefan Wagner, Otmar Schober, Michael Schäfers, Günter Haufe*

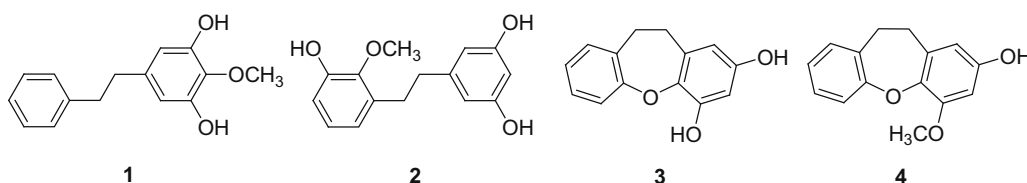


A series of new (S)-5-[1-(2-methoxymethylpyrrolidinyl)sulfonyl]isatins bearing fluorinated and non-fluorinated N-alkyl- and N-benzyl substituents has been synthesized and their inhibition potencies were assayed for recombinant human caspases-3 and -7. Among the most active inhibitors in this series are the *n*-propyl- and *n*-butyl derivatives as well as the corresponding terminal alcohols and fluorides.

Phenolic compounds with radical scavenging and cyclooxygenase-2 (COX-2) inhibitory activities from *Dioscorea opposita*

pp 2689–2694

Min Hye Yang, Kee Dong Yoon, Young-Won Chin, Ju Hyun Park, Jinwoong Kim*

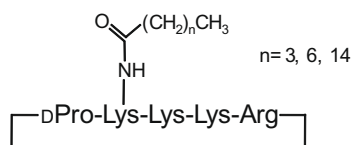


Two new dihydrostilbenes (**1**, **2**) and two new dibenzoxepins (**3**, **4**) together with 15 known compounds were isolated from the chloroform fraction of *Dioscorea opposita*. Of these, 3,3',5-trihydroxy-2'-methoxy-bibenzyl (**2**) showed most potent inhibitory activity against cyclooxygenase-2 (COX-2).

Modified low molecular weight cyclic peptides as mimetics of BDNF with improved potency, proteolytic stability and transmembrane passage in vitro

pp 2695–2702

Jordan M. Fletcher, Richard A. Hughes*



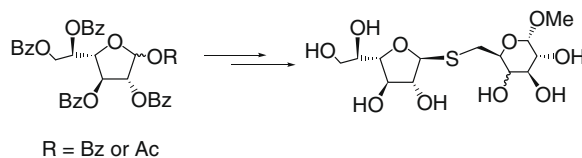
A series of hydrophobically-modified analogues of the peptide cyclo-[dPAKKR] were prepared and examined for their neurotropic activity, stability in plasma, and membrane permeability.



Thiodisaccharides with galactofuranose or arabinofuranose as terminal units: Synthesis and inhibitory activity of an *exo* β -D-galactofuranosidase

pp 2703–2711

Evangelina Repetto, Carla Marino, M. Laura Uhrig, Oscar Varela *

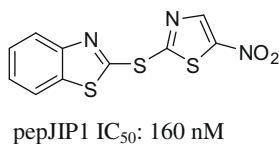


Thiodisaccharides having β -D-Galf or α -L-Araf as non-reducing units have been synthesized starting from peracetylated furanose derivatives. They were evaluated as inhibitors of the β -galactofuranosidase from *Penicillium fellutanum*.

**Discovery of 2-(5-nitrothiazol-2-ylthio)benzo[d]thiazoles as novel c-Jun N-terminal kinase inhibitors**

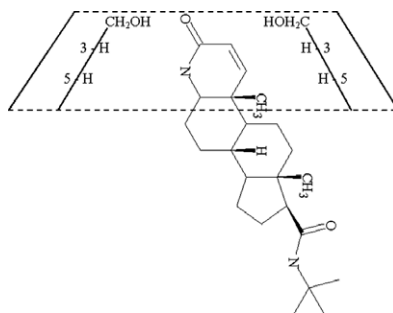
pp 2712–2717

Surya K. De, Li-Hsing Chen, John L. Stebbins, Thomas Machleidt, Megan Riel-Mehan, Russell Dahl, Vida Chen, Hongbin Yuan, Elisa Barile, Aras Emdadi, Ria Murphy, Maurizio Pellecchia *

**Binary and ternary inclusion complexes of finasteride in HP β CD and polymers: Preparation and characterization**

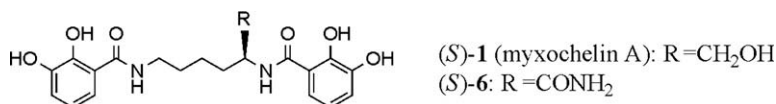
pp 2718–2723

Ana Carolina C. Asbahr*, Luzia Franco, Andersson Barison, Caroline W. P. Silva, Humberto G. Ferraz, Leticia N. C. Rodrigues

**Synthesis and evaluation of myxochelin analogues as antimetastatic agents**

pp 2724–2732

Satoshi Miyanaga, Hiroaki Sakurai, Ikuo Saiki, Hiroyasu Onaka, Yasuhiro Igarashi *

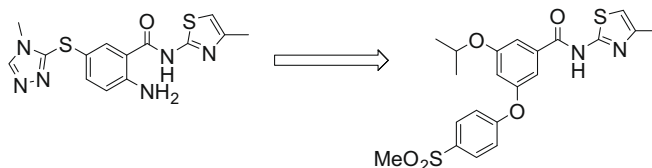


Structure–activity relationship of myxochelin analogues toward tumor cell invasion was investigated. Compound (S)-**6** showed the highest in vitro inhibition activity against invasion and suppression of metastasis in mouse.

Discovery of potent and orally active 3-alkoxy-5-phenoxy-*N*-thiazolyl benzamides as novel allosteric glucokinase activators

pp 2733–2743

Tomoharu Iino*, Daisuke Tsukahara, Kenji Kamata, Kaori Sasaki, Sumika Ohyama, Hideka Hosaka, Takuro Hasegawa, Masato Chiba, Yasufumi Nagata, Jun-ichi Eiki, Teruyuki Nishimura

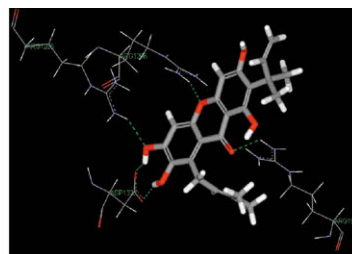
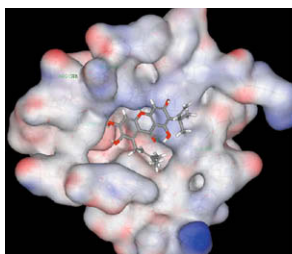
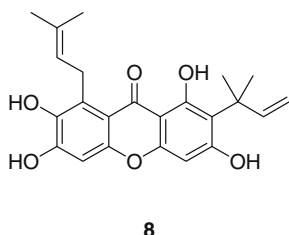


Identification and synthesis of novel 3-alkoxy-5-phenoxy-*N*-thiazolyl benzamide glucokinase activators are described.

Characteristic of neuraminidase inhibitory xanthenes from *Cudrania tricuspidata*

pp 2744–2750

Young Bae Ryu, Marcus J. Curtis-Long, Ji Won Lee, Jin Hyo Kim, Jun Young Kim, Kyu Young Kang, Woo Song Lee*, Ki Hun Park*



A series of xanthone derivatives from *Cudrania tricuspidata* are shown to display nanomolar inhibitor activity against neuraminidase as well as competitive inhibition modes.

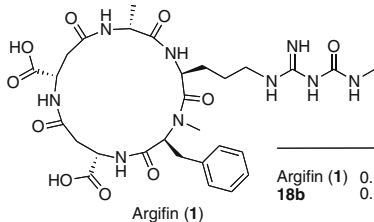


Argifin; efficient solid phase total synthesis and evaluation of analogues of acyclic peptide

pp 2751–2758

Toshiaki Sunazuka*, Akihiro Sugawara, Kanami Iguchi, Tomoyasu Hirose, Kenichiro Nagai, Yoshihiko Noguchi, Yoshifumi Saito, Tsuyoshi Yamamoto, Hideaki Ui, Hiroaki Gouda, Kazuro Shiomi, Takeshi Watanabe, Satoshi Omura*

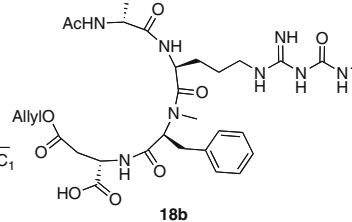
Solid Phase Total Synthesis



Structure Simplification along with increased activity

	SmChiA	IC ₅₀ (μM)	SmChiB	SmChiC ₁
Argifin (1)	0.025 ± 0.0024	6.4 ± 1.0	0.091 ± 0.0038	>30
18b	0.025 ± 0.0015	0.091 ± 0.0038	>30	>30

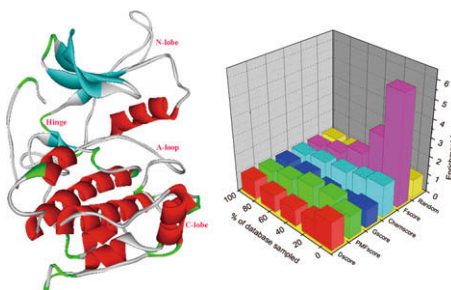
Discoverd more potent Acyclic peptide



IKKβ inhibitors identification part I: Homology model assisted structure based virtual screening

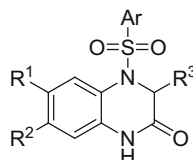
pp 2759–2766

Shanthi Nagarajan, Munikumar reddy Doddareddy, Hyunah Choo, Yong Seo Cho, Kwang-Seok Oh, Byung Ho Lee, Ae Nim Pae*



Synthesis and biological evaluation of N^4 -(hetero)arylsulfonylquinoxalinones as HIV-1 reverse transcriptase inhibitors

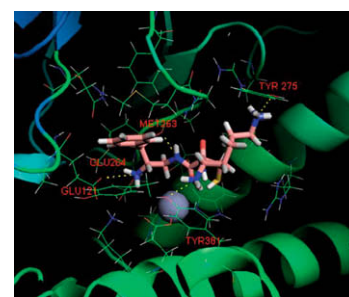
pp 2767–2774

Bailing Xu^{*}, Yan Sun, Ying Guo, Yingli Cao, Tao Yu

A series of novel N^4 -(hetero)arylsulfonylquinoxalinone derivatives were prepared in a straight and efficient way. Of all the synthesized compounds, five compounds exhibited potent anti-HIV-1 replication activities with IC_{50} value at the level of 10^{-7} mol/L. Preliminary structure–activity relationships were studied in details and that will shed light on the discovery of more potent non-nucleoside reverse-transcriptase inhibitors.

Design, synthesis and SAR studies of tripeptide analogs with the scaffold 3-phenylpropane-1,2-diamine as aminopeptidase N/CD13 inhibitors

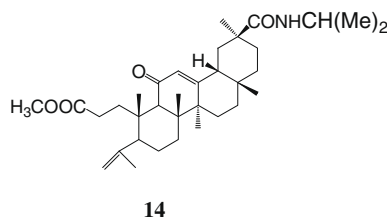
pp 2775–2784

Luqing Shang, Hao Fang, Huawei Zhu, Xuejian Wang, Qiang Wang, Jiajia Mu, Binghe Wang, Shiroh Kishioka, Wenfang Xu^{*}

The representative compound **B6** was built and docked into the active site of APN (PDB code: 2DQM) using *svbvl7.0*. The docking result was showed by PyMOL.

Synthesis, anti-inflammatory, and antioxidant activities of 18 β -glycyrrhetic acid derivatives as chemical mediators and xanthine oxidase inhibitors

pp 2785–2792

Dravidum Maitraie, Chi-Feng Hung, Huang-Yao Tu, Ya-Ting Liou, Bai-Luh Wei^{*}, Shyh-Chyun Yang, Jih-Pyang Wang, Chun-Nan Lin^{*}

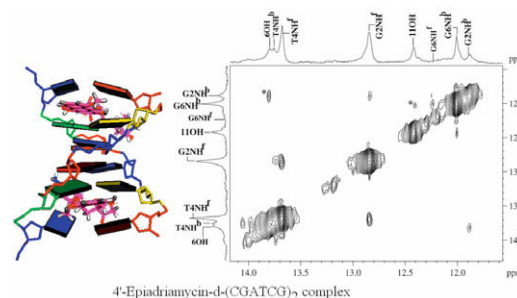
Twenty 18 β -glycyrrhetic acid (18 β -GA) derivatives **2–21** including 13 new 18 β -GA derivatives were synthesized and evaluated as anti-inflammatory and antioxidant agents.

Solution studies on the complex of 4'-epiadriamycin-d-(CGATCG)₂ followed by time-resolved fluorescence measurement, diffusion ordered spectroscopy and restrained molecular dynamics simulations

pp 2793–2811

Prashansa Agrawal, Sudhir Kumar Barthwal, Girjesh Govil, Ritu Barthwal^{*}

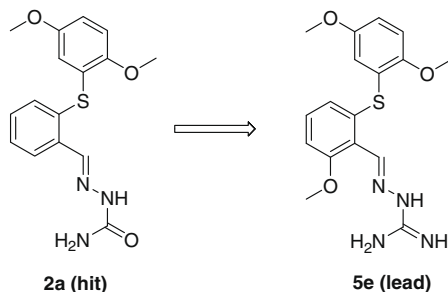
Binding of 4'-epiadriamycin, an anthracycline anticancer drug, with d-(CGATCG)₂ hexamer sequence to understand the drug–DNA interaction which is the primary step to comprehend the potent activity and low toxicity of this drug.

4'-Epiadriamycin-d-(CGATCG)₂ complex

Discovery and structure–activity relationships of (2-(arylthio)benzylideneamino)guanidines as a novel series of potent apoptosis inducers

pp 2852–2858

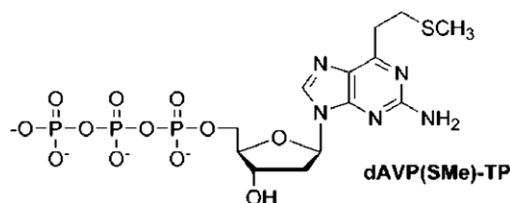
Han-Zhong Zhang, Candace Crogan-Grundy, Chris May, John Drewe, Ben Tseng, Sui Xiong Cai*



Incorporation of an inducible nucleotide analog into DNA by DNA polymerases

pp 2859–2863

Md. Monsur Ali, Shuhei Imoto, Yingfu Li*, Shigeki Sasaki*, Fumi Nagatsugi*

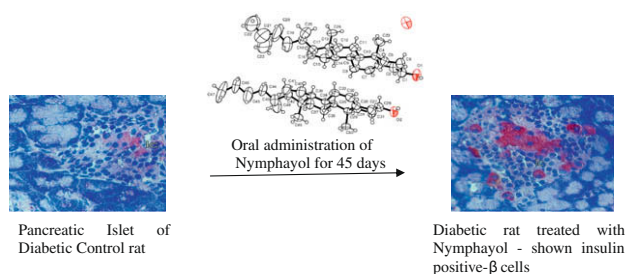


2'-Deoxyribosyl-2-amino-6-(2-methylthioethyl)purine nucleoside 5'-triphosphate (dAVP (SMe)-TP) was examined as a substrate of various DNA polymerases in DNA polymerization reactions to synthesize DNA containing this non-natural functional nucleotide.

Partial regeneration of β -cells in the islets of Langerhans by Nymphayol a sterol isolated from *Nymphaea stellata* (Willd.) flowers

pp 2864–2870

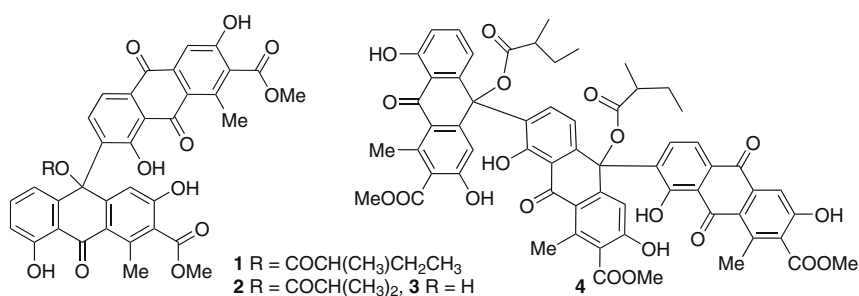
P. Subash-Babu, S. Ignacimuthu*, P. Agastian, Babu Varghese



Antiproliferative and antimalarial anthraquinones of *Scutia myrtina* from the Madagascar forest

pp 2871–2876

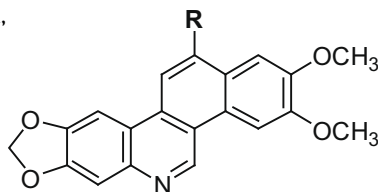
Yanpeng Hou, Shugeng Cao, Peggy J. Brodie, Martin W. Callmender, Fidisoa Ratovoson, Etienne A. Rakotobe, Vincent E. Rasamison, Michel Ratsimbason, John N. Alumasa, Paul D. Roepe, David G. I. Kingston*



12-Substituted 2,3-dimethoxy-8,9-methylenedioxybenzo[*i*]phenanthridines as novel topoisomerase I-targeting antitumor agents

pp 2877–2885

Wei Feng, Mavurapu Satyanarayana, Yuan-Chin Tsai,
Angela A. Liu, Leroy F. Liu, Edmond J. LaVoie*



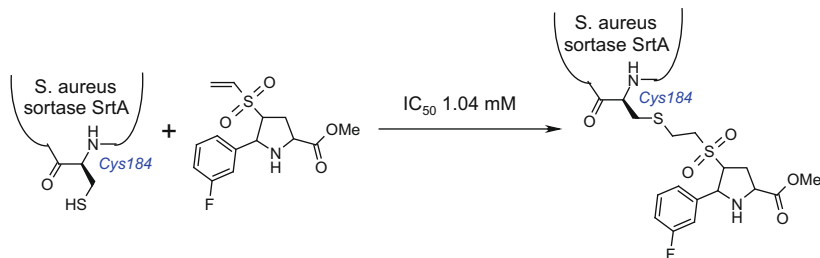
R = CH₂OH, CHO, CHCHNO₂, CH₂CH₂NO₂, CH₂CH₂NH₂,
CHOHCH₂CH₂CH₂N(CH₃)₂, CHCHCH₂CH₂N(CH₃)₂, CONH₂,
CONHCH₃, CON(CH₃)₂, and (CH₂)_nN(CH₃)₂ where n = 1–4

The synthesis and relative pharmacologic activities of several non-camptothecin TOP1-targeting agents structurally-related to ARC-111 was assessed.

Probing of the *cis*-5-phenyl proline scaffold as a platform for the synthesis of mechanism-based inhibitors of the *Staphylococcus aureus* sortase SrtA isoform

pp 2886–2893

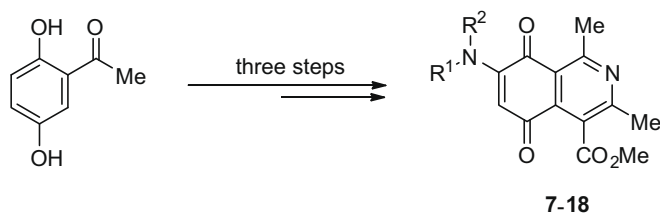
Konstantin V. Kudryavtsev*, Matthew L. Bentley, Dewey G. McCafferty



Studies on quinones. Part 45: Novel 7-aminoisoquinoline-5,8-quinone derivatives with antitumor properties on cancer cell lines

pp 2894–2901

Jaime A. Valderrama*, J. Andrea Ibacache, Verónica Arancibia, Jaime Rodriguez, Cristina Theoduloz

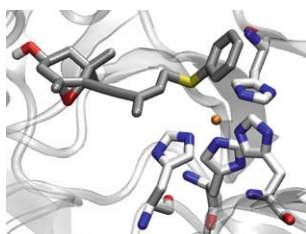


The synthesis of 7-aminoisoquinoline-5,8-quinone derivatives **7-18** (R¹ = phenyl, alkyl, H; R² = alkyl, H) and their cytotoxic activities on normal fibroblasts and three tumor cell lines is reported.

Sesquiterpene-like inhibitors of a 9-*cis*-epoxycarotenoid dioxygenase regulating abscisic acid biosynthesis in higher plants

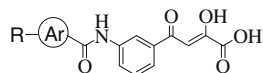
pp 2902–2912

Jason Boyd, Yuanzhu Gai, Ken M. Nelson, Erica Lukiwski, James Talbot, Mary K. Loewen, Stacey Owen, L. Irina Zaharia,
Adrian J. Cutler, Suzanne R. Abrams*, Michele C. Loewen



Amide-containing diketoacids as HIV-1 integrase inhibitors: Synthesis, structure–activity relationship analysis, and biological activity**pp 2913–2919**

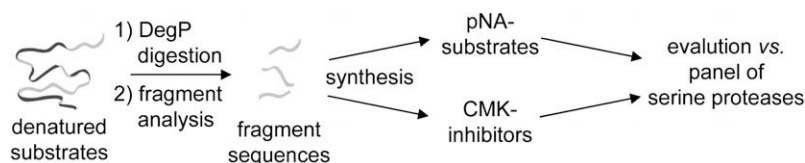
Hongcai Li, Chao Wang, Tino Sanchez, Yanmei Tan, Chunying Jiang, Nouri Neamati*, Guisen Zhao*



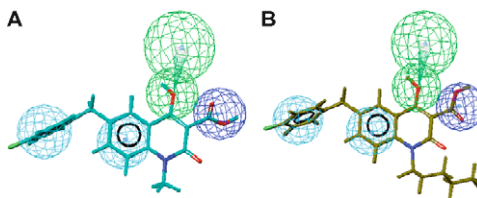
A series of novel amide-containing diketoacids were designed and synthesized to develop potent HIV integrase inhibitors. Their inhibition of HIV integrase was tested and the structure–activity relationships were discussed.

Selectivity profiling of DegP substrates and inhibitors**pp 2920–2924**

Patrick Hauske, Michael Meltzer, Christian Ottmann, Tobias Krojer, Tim Clausen, Michael Ehrmann*, Markus Kaiser*

**Design and synthesis of novel dihydroquinoline-3-carboxylic acids as HIV-1 integrase inhibitors****pp 2925–2935**

Mario Sechi*, Giuseppe Rizzi, Alessia Bacchi, Mauro Carcelli, Dominga Rogolino, Nicolino Pala, Tino W. Sanchez, Laleh Taheri, Raveendra Dayam, Nouri Neamati*

**OTHER CONTENTS****Erratum****p 2936****Bioorganic & Medicinal Chemistry Reviews and Perspectives****pp 2937–2939****Instructions to contributors****p I**

*Corresponding author

i+ Supplementary data available via ScienceDirect

COVER

DegP represents an unusual protease-chaperone molecular machine. Substrates and inhibitors of this important enzyme were derived from sequences of digestion fragments and profiled for their selectivity vs. a panel of serine proteases. The figure was created using X-ray data of DegP (PDB code: 1KY9) deposited in the protein data bank from the following publication: Krojer, T., Garrido-Franco, M., Huber, R., Ehrmann, M., Clausen, T. (2002) Crystal structure of DegP (HtrA) reveals a new protease-chaperone machine. *Nature* 416: 455–459. [Hauske, P.; Meltzer, M.; Ottmann, C.; Krojer, T.; Clausen, T.; Ehrmann, M.; Kaiser, M. *Bioorg. Med. Chem.* **2009**, 17, 2920–2924].

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ISSN 0968-0896