

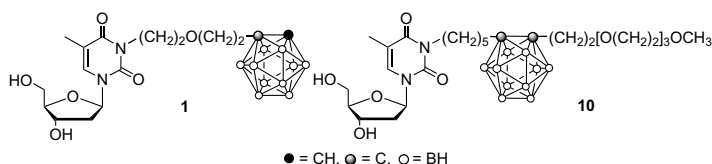
Contents

ARTICLES

Synthesis of ethyleneoxide modified 3-carboranyl thymidine analogues and evaluation of their biochemical, physicochemical, and structural properties

pp 4769–4781

Jayaseharan Johnsamuel, Nisha Lakhi, Ashraf S. Al-Madhoun, Youngjoo Byun, Junhua Yan, Staffan Eriksson and Werner Tjarks*

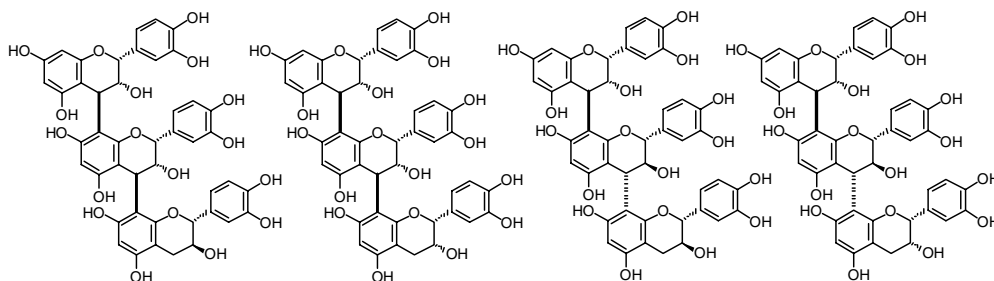


A library of eleven 3-carboranyl thymidine analogues (3CTAs), all of which containing hydrophilic ethyleneoxide moieties, were synthesized and their biochemical and physicochemical properties were evaluated.

Systematic synthesis of four epicatechin series procyanidin trimers and their inhibitory activity on the Maillard reaction and antioxidant activity

pp 4783–4790

Akiko Saito,* Yuki Doi, Akira Tanaka, Nobuyasu Matsuura, Makoto Ubukata and Noriyuki Nakajima*

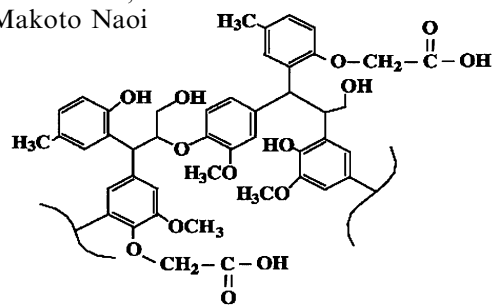


A highly bioactive lignophenol derivative from bamboo lignin exhibits a potent activity to suppress apoptosis induced by oxidative stress in human neuroblastoma SH-SY5Y cells

pp 4791–4801

Yukihiro Akao,* Norio Seki, Yoshihito Nakagawa, Hong Yi, Kenji Matsumoto, Yukie Ito, Kuniyasu Ito, Masamitsu Funaoka, Wakako Maruyama, Makoto Naoi and Yoshinori Nozawa

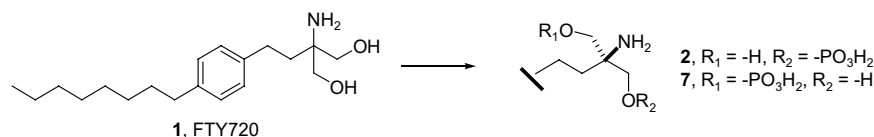
A lignocresol derivative from bamboo (lig-8) exhibited a potent neuroprotective activity against hydrogen peroxide (H₂O₂)-induced apoptosis in human neuroblastoma cell line SH-SY5Y by preventing the caspase-3 activation via either caspase-8 or caspase-9.



Synthesis, stereochemical determination and biochemical characterization of the enantiomeric phosphate esters of the novel immunosuppressive agent FTY720

pp 4803–4807

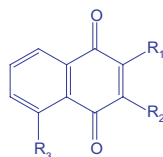
Jeffrey J. Hale,* Lin Yan, William E. Neway, Richard Hajdu, James D. Bergstrom, James A. Milligan, Gan-Ju Shei, Gary L. Chrebet, Rosemary A. Thornton, Deborah Card, Mark Rosenbach, Hugh Rosen and Suzanne Mandala



Quinones as antimycobacterial agents

pp 4809–4813

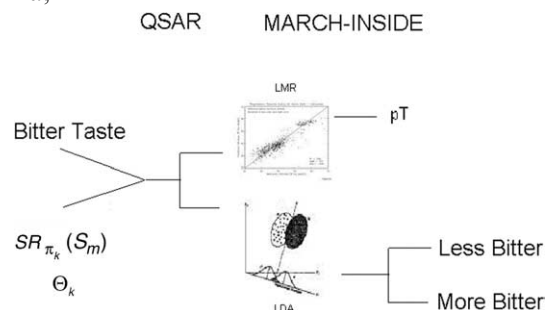
Thuyanh Tran, Ekta Saheba, Ariana V. Arcerio, Violeta Chavez, Qing-yi Li, Luis E. Martinez and Todd P. Primm*



Stochastic-based descriptors studying peptides biological properties: modeling the bitter tasting threshold of dipeptides

pp 4815–4822

Ronal Ramos de Armas,* Humberto González Díaz, Reinaldo Molina, Maykel Pérez González and Eugenio Uriarte

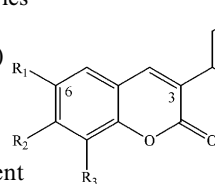


New 3-piperonylcoumarins as inhibitors of glycosomal glyceraldehyde-3-phosphate dehydrogenase (gGAPDH) from *Trypanosoma cruzi*

pp 4823–4833

Anderson Aparecido de Marchi, Marcelo Santos Castilho, Paulo Gustavo Barboni Nascimento, Fernando Costa Archanjo, Gino Del Ponte, Glaucius Oliva and Mônica Tallarico Pupo*

This article describes the synthesis and inhibitory activities of a series of new 3-piperonylcoumarins, designed as inhibitors of glycosomal glyceraldehyde-3-phosphate dehydrogenase (gGAPDH) from *Trypanosoma cruzi*. SAR studies, performed by electronic indices methodology (EIM), clustered the molecules in different groups due to the chemical substitutions regarding the biological activity. Molecular modeling studies by docking suggested a different binding mode for the most active derivatives, when compared to natural hit chalepin. Moreover, the coumarin ring seems to act only as a spacer group.

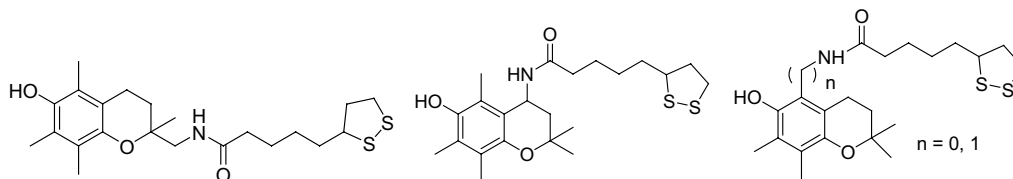


- 2a $R_1 = NO_2$, $R_2 = R_3 = H$
- 2b $R_1 = OAc$, $R_2 = R_3 = H$
- 2c $R_2 = OAc$, $R_1 = R_3 = H$
- 2d $R_3 = OAc$, $R_1 = R_2 = H$
- 2e $R_1 = R_2 = R_3 = H$
- 3b $R_1 = OH$, $R_2 = R_3 = H$
- 3c $R_2 = OH$, $R_1 = R_3 = H$
- 3d $R_3 = OH$, $R_1 = R_2 = H$
- 4 $R_1 = NH_2$, $R_2 = R_3 = H$
- 5a $R_1 = (1E)$ -1H-pyrrol-2-ylmethylamino, $R_2 = R_3 = H$
- 5b $R_1 = (1E)$ -2-furylmethylamino, $R_2 = R_3 = H$
- 5c $R_1 = (1E)$ -thien-2-ylmethylamino, $R_2 = R_3 = H$
- 6 $R_1 = (1E)$ -1H-indol-3-ylmethylamino, $R_2 = R_3 = H$
- 7 $R_1 = (1E)$ -pyridin-2-ylmethylamino, $R_2 = R_3 = H$

Synthesis of chroman analogues of lipoic acid and evaluation of their activity against reperfusion arrhythmias

pp 4835–4841

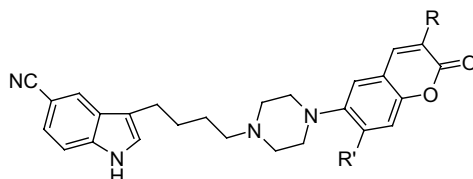
Maria Koufaki,* Anastasia Detsi, Elissavet Theodorou, Christina Kiziridi, Theodora Calogeropoulou, Athanasios Vassilopoulos, Angeliki P. Kourounakis, Eleni Rekka, Panos N. Kourounakis, Catherine Gaitanaki and Panagiota Papazafiri



Dual 5-HT_{1A} agonists and 5-HT re-uptake inhibitors by combination of indole-butyl-amine and chromenonyl-piperazine structural elements in a single molecular entity

pp 4843–4852

Timo Heinrich,* Henning Böttcher, Kai Schiemann, Günter Hölzemann, Michael Schwarz, Gerd D. Bartoszyk, Christoph van Amsterdam, Hartmut E. Greiner and Christoph A. Seyfried

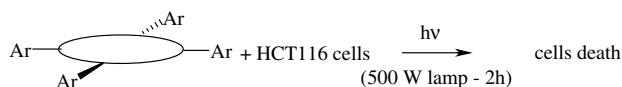


A series of compounds as dual serotonin re-uptake inhibitor and 5-HT_{1A} receptor agonist was found to increase central serotonin levels in rat brain to a greater extent than established antidepressants.

Photodynamic effects of porphyrin and chlorin photosensitizers in human colon adenocarcinoma cells

pp 4853–4860

Stefano Banfi,* Enrico Caruso, Stefania Caprioli, Luigi Mazzagatti, Gianfranco Canti, Raffaella Ravizza, Marzia Gariboldi and Elena Monti



Porphyrins and Chlorins

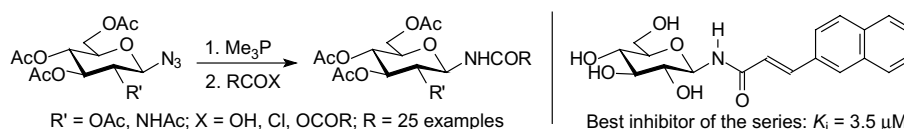
Ar = 3-methoxyphenyl; 4-methoxyphenyl; 3,4,5-trimethoxyphenyl; 3-hydroxyphenyl; 4-hydroxyphenyl; 3,4,5-trihydroxyphenyl; 4-sulfonamidophenyl.

A series of tetraaryl porphyrins and chlorins were synthesized and tested for photodynamic activity in human colon adenocarcinoma cells.

Synthesis of *N*-(β-D-glucopyranosyl)- and *N*-(2-acetamido-2-deoxy-β-D-glucopyranosyl) amides as inhibitors of glycogen phosphorylase

pp 4861–4870

Zoltán Györgydeák,* Zsuzsa Hadady, Nóra Felföldi, Attila Krakomperger, Veronika Nagy, Marietta Tóth, Attila Brunyánszki, Tibor Docsa, Pál Gergely and László Somsák*

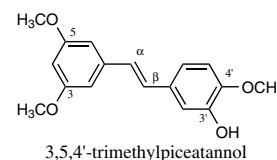


Anti-allergic activity of stilbenes from Korean rhubarb (*Rheum undulatum* L.): structure requirements for inhibition of antigen-induced degranulation and their effects on the release of TNF- α and IL-4 in RBL-2H3 cells

pp 4871–4876

Hisashi Matsuda, Supinya Tewtrakul, Toshio Morikawa and Masayuki Yoshikawa*

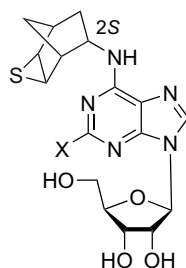
Stilbenes isolated from the rhizomes of *Rheum undulatum* (Korean rhubarb) and the related compounds were investigated on their anti-allergic activities. The results revealed that 3,5,4'-trimethylpiceatannol exhibited the most potent inhibition against β -hexosaminidase release, as a marker of degranulation in RBL-2H3 cells, with IC_{50} of 2.1 μ M, followed by trimethylresveratrol (IC_{50} = 5.1 μ M). Structural requirements of stilbenes for the activity are as follows: (1) The oxygen functions ($-OCH_3$, $-OH$) are essential and their positions on aromatic rings are important for the activity, especially that of methoxyl groups; (2) the α - β double bond increased the activity; (3) the glycoside moiety dramatically decreased the activity; and (4) substitution at the 3'-position of trimethylresveratrol (3,5,4'-trimethoxystilbene) was preferably $OH > H > OCH_3$ for the activity. Piceatannol, 3,5,4'-trimethylpiceatannol, resveratrol, and trimethylresveratrol also significantly inhibited antigen-induced release of TNF- α and IL-4 in RBL-2H3 cells.



New potent and selective A_1 adenosine receptor agonists

pp 4877–4884

Sally A. Hutchinson, Stephen P. Baker, Joel Linden and Peter J. Scammells*

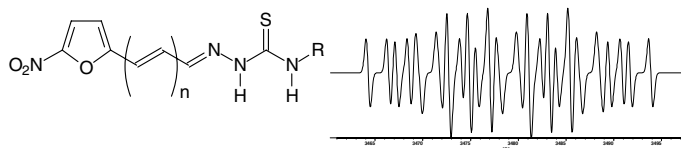


Thirane analogs of ENA do have been synthesised and found to be extremely potent and selective A_1 adenosine receptor agonists.

In vitro activity and mechanism of action against the protozoan parasite *Trypanosoma cruzi* of 5-nitrofuryl containing thiosemicarbazones

pp 4885–4893

Gabriela Aguirre, Lucía Boiani, Hugo Cerecetto,* Marcelo Fernández, Mercedes González,* Ana Denicola, Lucía Otero, Dinorah Gambino, Carolina Rigol, Claudio Olea-Azar and Mario Faundez

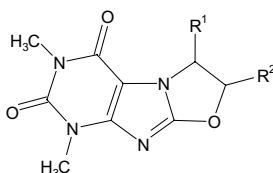


New 5-nitrofuryl containing thiosemicarbazone derivatives with anti-*Trypanosoma cruzi* are reported. Mechanism of action was studied using ESR spectroscopy and theoretical calculations.

Tricyclic oxazolo[2,3-f]purinediones: potency as adenosine receptor ligands and anticonvulsants

pp 4895–4908

Anna Drabczyńska, Christa E. Müller, Britta Schumacher, Sonja Hinz, Janina Karolak-Wojciechowska, Barbara Michalak, Elżbieta Pękala and Katarzyna Kieć-Kononowicz*

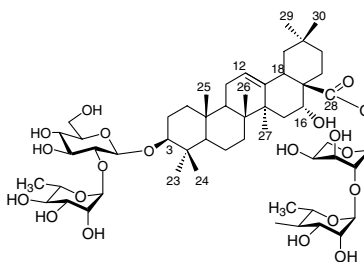


A series of tricyclic mono- or disubstituted oxazolo[2,3-f]purinediones was synthesized and evaluated for their adenosine receptor affinity and anticonvulsant activity. Mainly selective adenosine A_{2A} receptor antagonists were identified. A 7-benzyl-substituted derivative (**13**) showed good adenosine A_1 receptor affinity. Anticonvulsant activity was observed for certain compounds in MES and ScMet tests, but did not correlate with adenosine receptor affinity.

Astersedifolioside A–C, three new oleanane-type saponins with antiproliferative activity

pp 4909–4915

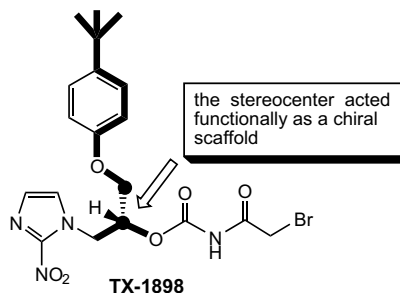
Gabriella Corea, Maria Iorizzi, Virginia Lanzotti,* Maria Cammareri, Clara Conicella, Chiara Laezza and Maurizio Bifulco



Angiogenesis inhibitor TX-1898: syntheses of the enantiomers of sterically diverse haloacetylcarbamoyl-2-nitroimidazole hypoxic cell radiosensitizers

pp 4917–4927

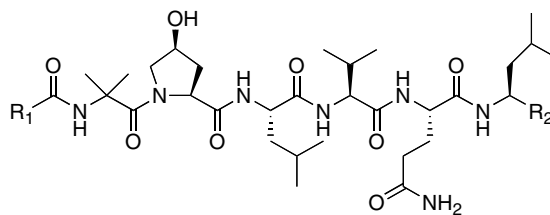
Cheng-Zhe Jin, Hideko Nagasawa, Mariko Shimamura, Yoshihiro Uto, Seiichi Inayama, Yoshio Takeuchi, Kenneth L. Kirk and Hitoshi Hori*



Synthesis and structure–activity relationships of the halovirs, antiviral natural products from a marine-derived fungus

pp 4929–4936

David C. Rowley,* Sara Kelly, Paul Jensen and William Fenical



Structure–affinity studies for a novel series of homochiral naphtho and tetrahydronaphtho analogues of α_1 antagonist WB-4101

pp 4937–4951

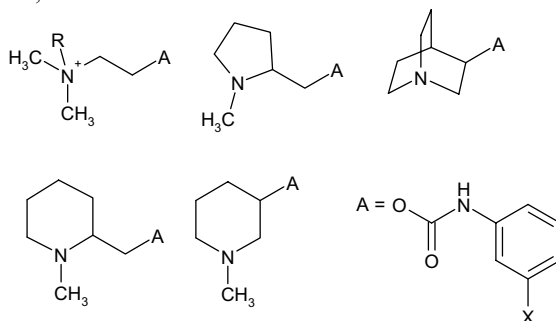
Cristiano Bolchi, Paolo Catalano, Laura Fumagalli, Marco Gobbi, Marco Pallavicini, Alessandro Pedretti, Luigi Villa, Giulio Vistoli and Ermanno Valoti*

	<table> <tr> <th></th> <th>R₁</th> <th>R₂</th> <th>R₃</th> </tr> <tr> <td>2</td> <td>-(CH=CH)₂</td> <td></td> <td>2,6-dimethoxyphenyl</td> </tr> <tr> <td>3</td> <td>-(CH₂CH₂)₂</td> <td></td> <td>"</td> </tr> <tr> <td>4</td> <td>H</td> <td>H</td> <td>1-naphthyl</td> </tr> <tr> <td>5</td> <td>H</td> <td>H</td> <td>2-naphthyl</td> </tr> </table>		R ₁	R ₂	R ₃	2	-(CH=CH) ₂		2,6-dimethoxyphenyl	3	-(CH ₂ CH ₂) ₂		"	4	H	H	1-naphthyl	5	H	H	2-naphthyl	<table> <tr> <th></th> <th>R₁</th> <th>R₂</th> <th>R₃</th> </tr> <tr> <td>6</td> <td>H</td> <td>H</td> <td>2-methoxy-1-naphthyl</td> </tr> <tr> <td>7</td> <td>H</td> <td>H</td> <td>1-methoxy-2-naphthyl</td> </tr> <tr> <td>8</td> <td>H</td> <td>H</td> <td>3-methoxy-2-naphthyl</td> </tr> </table>		R ₁	R ₂	R ₃	6	H	H	2-methoxy-1-naphthyl	7	H	H	1-methoxy-2-naphthyl	8	H	H	3-methoxy-2-naphthyl
	R ₁	R ₂	R ₃																																			
2	-(CH=CH) ₂		2,6-dimethoxyphenyl																																			
3	-(CH ₂ CH ₂) ₂		"																																			
4	H	H	1-naphthyl																																			
5	H	H	2-naphthyl																																			
	R ₁	R ₂	R ₃																																			
6	H	H	2-methoxy-1-naphthyl																																			
7	H	H	1-methoxy-2-naphthyl																																			
8	H	H	3-methoxy-2-naphthyl																																			
1 (WB-4101: R ₁ =R ₂ =H, R ₃ =2,6-dimethoxyphenyl)																																						

Synthesis and evaluation of phenylcarbamate derivatives as ligands for nicotinic acetylcholine receptors

pp 4953–4962

Daniela Gündisch,* Matthias Andrä, Lenka Munoz and Maria Cristina Tilotta

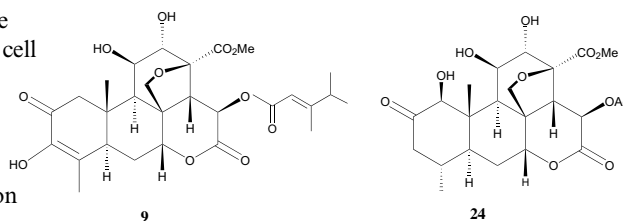


Multidrug-resistant cancer cell susceptibility to cytotoxic quassinoids, and cancer chemopreventive effects of quassinoids and canthin alkaloids

pp 4963–4968

Chihiro Murakami, Narihiko Fukamiya,* Sadaaki Tamura, Masayoshi Okano, Kenneth F. Bastow, Harukuni Tokuda, Teruo Mukainaka, Hoyoky Nishino and Kuo-Hsiung Lee

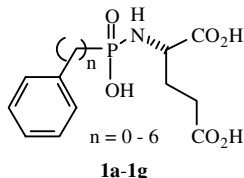
Twenty-three quassinoids (**1–23**) from Simaroubaceous plants were evaluated for cytotoxicity against three multidrug-resistant cancer cell lines, KB-VIN, KB-7d, and KB-CPT. Nine compounds (**2–7** and **9–11**) showed significant cytotoxicity in all three cell lines. In addition, six quassinoid derivatives (**24–29**) and four canthin alkaloids (**30–33**) were examined for their inhibitory effects on TPA-induced Epstein–Barr virus early antigen (EBV-EA) activation as cancer chemopreventive agents. All of these compounds demonstrated significant inhibitory effects against EBV-EA activation.



Probing for a hydrophobic a binding register in prostate-specific membrane antigen with phenylalkylphosphonamidates

pp 4969–4979

Jack Maung, Jeremy P. Mallari, Teri A. Girtsman, Lisa Y. Wu, Jennifer A. Rowley, Nicholas M. Santiago, Alan N. Brunelle and Clifford E. Berkman*



A series of phenylalkylphosphonamidate derivatives of glutamic acid were synthesized and evaluated for their inhibitory potencies against PSMA. The greatest inhibitory potency was observed for the inhibitors **1f** ($n = 5$) and **1g** ($n = 6$) suggesting the presence of a hydrophobic binding register remote from the substrate recognition architecture in the active site of PSMA.

Antibody-catalyzed oxidative degradation of nicotine using riboflavin

pp 4981–4987

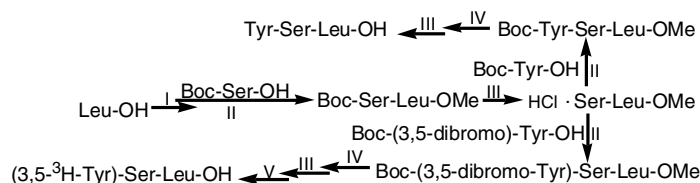
Tobin J. Dickerson, Noboru Yamamoto and Kim D. Janda*



The synthesis, distribution, and anti-hepatic cancer activity of YSL

pp 4989–4994

Wenfeng Ding, Jiali Zhang, Zhi Yao, Rong Lu, Dezhu Wu, Ginfu Li, Zilong Shen, Yingji Sun, Gang Lin, Chao Wang, Ming Zhao and Shiqi Peng*

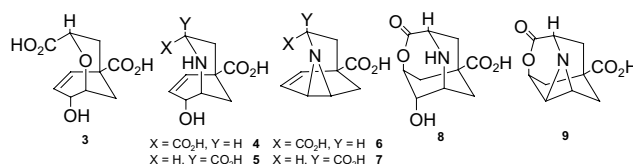


(I) HCl/CH₃OH; (II) DCC/HOBt/NMM with corresponding carboxyl component; (III) HCl/CH₃CO₂C₂H₅ (6 mol/L); (IV) NaOH/H₂O/CH₃OH; (V) ³H₂ and 10% Pd/C.

Design, synthesis, and evaluation of aza inhibitors of chorismate mutase

pp 4995–5010

Mark E. Hediger



The detailed information pertaining to this panel of aza inhibitors is presented.

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Contributors to this issue

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Instructions to contributors

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*Corresponding author

COVER

2004: Overlaps of the eight known aldolase alpha-beta barrels in 2-deoxyribose-5-phosphate aldolase (DERA). Ribbon model for DERA is shown in green, with key Lys residues capable of Schiff base formation highlighted in stick figure. Reactive Lys167 is shown in yellow. DeSantis, G.; Liu, J.; Clark, D. P.; Heine, A.; Wilson, I. A.; and Wong, C.-H. *Bioorganic & Medicinal Chemistry* 2003, 11, 43–52.

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