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# Bioorganic & Medicinal Chemistry

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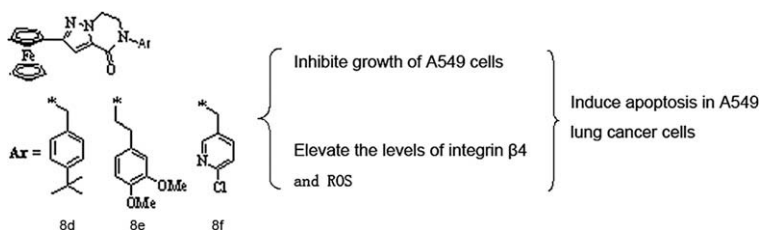
## Bioorganic & Medicinal Chemistry Vol. 16, No. 20, 2008

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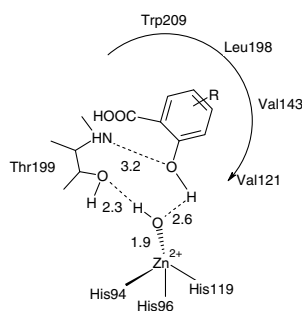
Xiao-Hong Pan, Xia Liu, Bao-Xiang Zhao\*, Yong-Sheng Xie, Dong-Soo Shin, Shang-Li Zhang, Jing Zhao, Jun-Ying Miao\*



5-Alkyl-2-ferrocenyl-6,7-dihydropyrazolo[1,5-*a*]pyrazin-4(5*H*)-one derivatives **8d**, **8e** and **8f** induced apoptosis in A549 cancer cells and elevated the levels of integrin  $\beta 4$  and ROS.

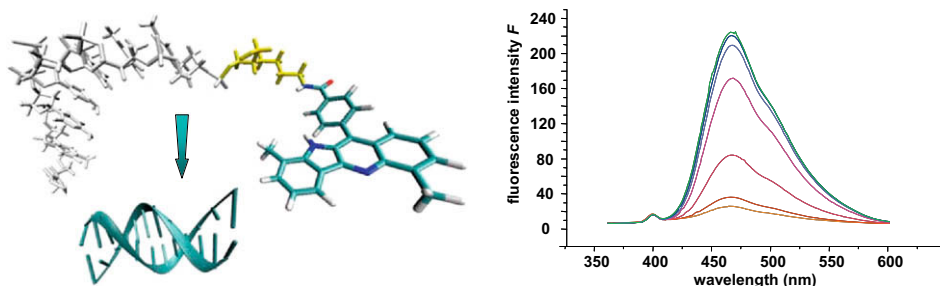
- In vitro inhibition of salicylic acid derivatives on human cytosolic carbonic anhydrase isozymes I and II** pp 9101–9105

Esra Bayram, Murat Senturk, O. Irfan Kufrevioglu\*, Claudiu T. Supuran\*



- Spectroscopic studies on the formation and thermal stability of DNA triplexes with a benzoannulated  $\delta$ -carboline-oligonucleotide conjugate** pp 9106–9112

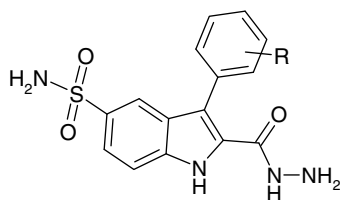
Andrea Eick, Zhou Xiao, Peter Langer, Klaus Weisz\*



**Carbonic anhydrase inhibitors: Synthesis and inhibition studies against mammalian isoforms I–XV with a series of 2-(hydrazinocarbonyl)-3-substituted-phenyl-1*H*-indole-5-sulfonamides**

pp 9113–9120

Özlen Güzel, Alessio Innocenti, Andrea Scozzafava, Aydın Salman, Seppo Parkkila, Mika Hilvo, Claudiu T. Supuran\*

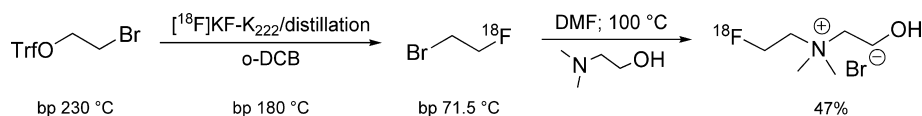


R = H, Me, F, Cl, Br, OMe, etc.

**Simplified fast and high yielding automated synthesis of [<sup>18</sup>F]fluoroethylcholine for prostate cancer imaging**

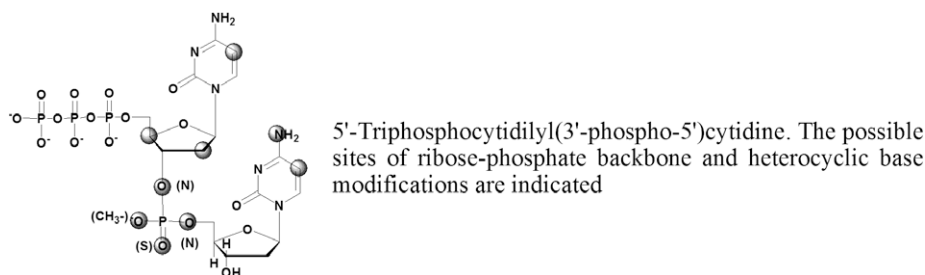
pp 9121–9126

M. Zuhayra\*, A. Alfteimi, L. Papp, U. Lützen, A. Lützen, C. Von Forstner, B. Meller, E. Henze


**Design and synthesis of dinucleotide 5'-triphosphates with expanded functionality**

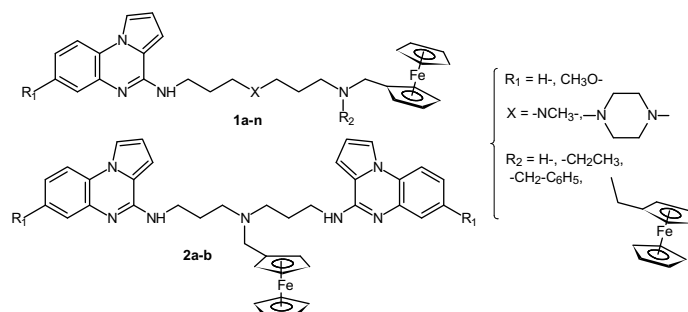
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Tatiana V. Abramova\*, Svetlana V. Vasileva, Ludmila S. Koroleva, Nina S. Kasatkina, Vladimir N. Silnikov


**New ferrocenic pyrrolo[1,2-*a*]quinoxaline derivatives: Synthesis, and in vitro antimalarial activity**

pp 9133–9144

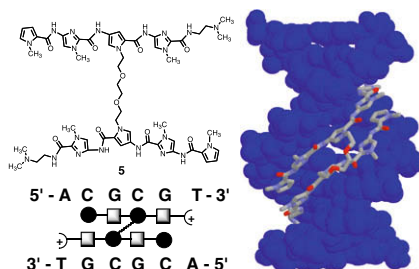
Jean Guillon\*, Stéphane Moreau, Elisabeth Mouray, Véronique Sinou, Isabelle Forfar, Solene Belisle Fabre, Vanessa Desplat, Pascal Millet, Daniel Parzy, Christian Jarry, Philippe Grellier



### Sequence specific and high affinity recognition of 5'-ACGCGT-3' by rationally designed pyrrole-imidazole H-pin polyamides: Thermodynamic and structural studies

pp 9145–9153

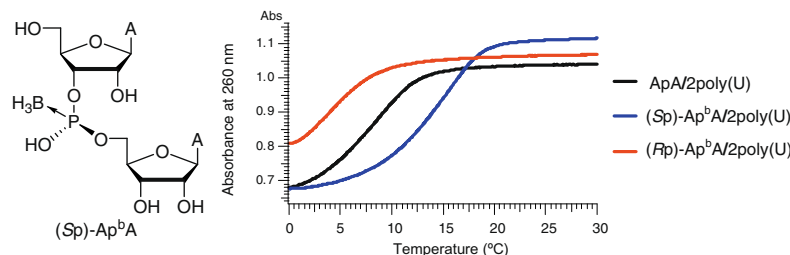
Hilary Mackay, Toni Brown, Peter B. Uthe, Laura Westrate, Alan Sielaff, Justin Jones, James P. Lajiness, Jerome Kluza, Caroline O'Hare, Binh Nguyen, Zach Davis, Chrystal Bruce, W. David Wilson, John A. Hartley, Moses Lee\*



### Chemical synthesis of diastereomeric diadenosine boranophosphates (Ap<sup>b</sup>A) from 2'-O-(2-cyanoethoxymethyl)adenosine by the boranophosphotriester method

pp 9154–9160

Yukiko Enya, Seigo Nagata\*, Yutaka Masutomi, Hidetoshi Kitagawa, Kazuchika Takagaki, Natsuhisa Oka, Takeshi Wada, Tadaaki Ohgi, Junichi Yano

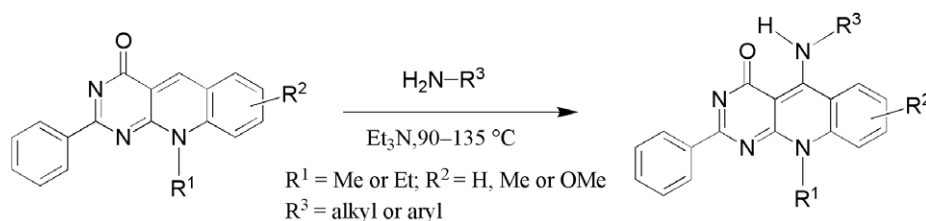


*T<sub>m</sub>* values of dimer/2poly(U) complexes revealed that presumptive (Sp)-Ap<sup>b</sup>A had a much higher and presumptive (Rp)-Ap<sup>b</sup>A a much lower affinity for poly(U) than the natural dimer did, ApA. In contrast, the *T<sub>m</sub>* values of the dimer/2poly(dT) complexes were all similar.

### Antitumor studies. Part 5: Synthesis, antitumor activity, and molecular docking study of 5-(monosubstituted amino)-2-deoxy-2-phenyl-5-deazaflavins

pp 9161–9170

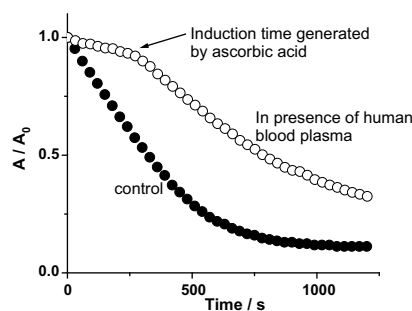
Ajaya R. Shrestha, Hamed I. Ali, Noriyuki Ashida, Tomohisa Nagamatsu\*



### Antioxidant capacity of human blood plasma and human urine: Simultaneous evaluation of the ORAC index and ascorbic acid concentration employing pyrogallol red as probe

pp 9171–9175

P. Torres, P. Galleguillos, E. Lissi, C. López-Alarcón\*

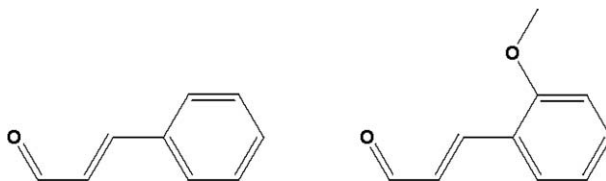


The ORAC methodology using pyrogallol red as probe has been employed to estimate the antioxidant capacity and simultaneously, the concentration of ascorbic acid in human blood plasma and human urine.

### Aldehydic components of Cinnamon bark extract suppresses RANKL-induced osteoclastogenesis through NFATc1 downregulation

pp 9176–9183

Kentarō Tsuji-Naito\*



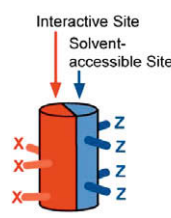
*Cinnamomum zeylanicum* exhibited the strong inhibitory effects on osteoclastogenesis and that its mechanism of action involved the suppression of NFATc1-mediated signal transduction. In addition, cinnamaldehyde and 2-methoxycinnamaldehyde were identified as its active components.



### Identification of minimal sequence for HIV-1 fusion inhibitors

pp 9184–9187

Hiroki Nishikawa, Shinya Oishi, Mizuno Fujita, Kentaro Watanabe, Rei Tokiwa, Hiroaki Ohno, Eiichi Kodama, Kazuki Izumi, Keiko Kajiwar, Takeshi Naitoh, Masao Matsuoka, Akira Otaka, Nobutaka Fujii\*

	Sequences	Anti-HIV EC <sub>50</sub> (nM)
	WMEWDREINNYTSLIHSLEESQNNQEKNEQELL	0.68
	WEEWDKKEEYTKKIEELIKKSEEQQKKNEEELKK	0.39
	WEEWDKKEEYTKKIEELIKKSEEQQKKNN	0.46
	W <sup>a</sup> EEWD <sup>a</sup> KKEEYTKKIEELIKKSEEQQKKNN	0.54

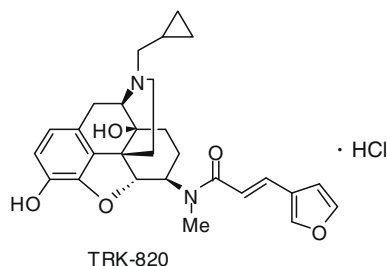
<sup>a</sup>: 2-aminoisobutyric acid (Aib)

Minimal sequence of potential HIV-1 fusion inhibitors was identified using glycoprotein gp41-derived peptides containing  $\alpha$ -helix-inducible EK motifs. One of the N-terminal motifs was replaced with an  $\alpha$ -helix-inducible motif containing 2-aminoisobutyric acids.

### Design, synthesis, and structure–activity relationship of novel opioid $\kappa$ -agonists

pp 9188–9201

Koji Kawai, Jun Hayakawa, Toru Miyamoto, Yoshifumi Imamura, Shinichi Yamane, Hisanori Wakita, Hideaki Fujii, Kuniaki Kawamura, Hirotohi Matsuura, Naoki Izumimoto, Ryosuke Kobayashi, Takashi Endo, Hiroshi Nagase\*

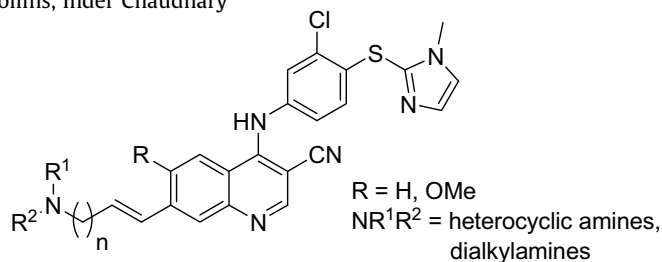


We designed and synthesized a novel opioid  $\kappa$ -agonist, TRK-820, which showed potent analgesic activity without addiction and aversion.

### 4-Anilino-7-alkenylquinoline-3-carbonitriles as potent MEK1 kinase inhibitors

pp 9202–9211

Dan M. Berger\*, Minu Dutia, Dennis Powell, Middleton B. Floyd, Nancy Torres, Robert Mallon, Donald Wojciechowicz, Steven Kim, Larry Feldberg, Karen Collins, Inder Chaudhary

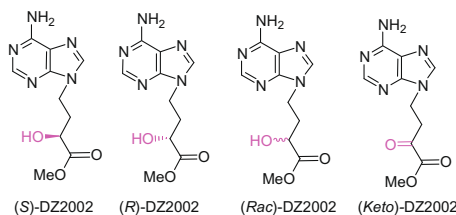


A series of 7-alkenyl substituted 4-anilino-3-quinolinecarbonitriles were prepared and evaluated as MEK1 kinase inhibitors. One analog (R = H, NR<sup>1</sup>R<sup>2</sup> = N-ethylpiperazine, n = 2) was active in an H358 (lung) xenograft study when dosed orally.

**Synthesis and biological evaluation of immunosuppressive agent DZ2002 and its stereoisomers**

pp 9212–9216

Yang-Ming Zhang, Yu Ding, Wei Tang, Wei Luo, Min Gu, Wei Lu\*, Jie Tang, Jian-Ping Zuo\*, Fa-Jun Nan\*

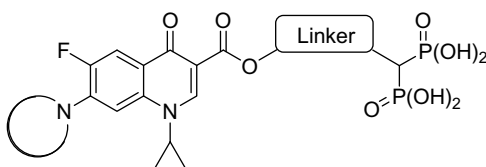


DZ2002 and its stereoisomers were efficiently prepared and evaluated on their potency against SAHase and mixed lymphocyte reaction (MLR). In accordance with respective inhibitory potency of SAHase, the immunosuppressive potency order was demonstrated as (S)-DZ2002 > (Rac)-DZ2002 > (R)-DZ2002 > (Keto)-DZ2002. These results indicate that the 2'-chiral center of DZ2002 plays a critical role for their function. Therefore, quality control to prepare optical (S)-DZ2002 is necessary for further biological studies.

**Bisphosphonated fluoroquinolone esters as osteotropic prodrugs for the prevention of osteomyelitis**

pp 9217–9229

Kelly S. E. Tanaka, Tom J. Houghton, Ting Kang, Evelyne Dietrich, Daniel Delorme, Sandra S. Ferreira, Laurence Caron, Frederic Viens, Francis F. Arhin, Ingrid Sarmiento, Dario Lehoux, Ibtihal Fadhil, Karine Laquerre, Jing Liu, Valérie Ostiguy, Hugo Poirier, Gregory Moeck, Thomas R. Parr Jr., Adel Rafai Far\*

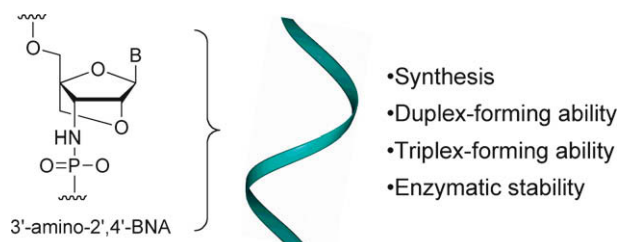


Bisphosphonated fluoroquinolone esters were synthesized and evaluated in vitro. These compounds were found to display strong affinity for bone and their ability to regenerate the parent drug was tailored. The efficacy of a representative class of these prodrugs as prophylactic treatments in a rat model of osteomyelitis is presented.

**Synthesis and properties of 3'-amino-2',4'-BNA, a bridged nucleic acid with a N3'→P5' phosphoramidate linkage**

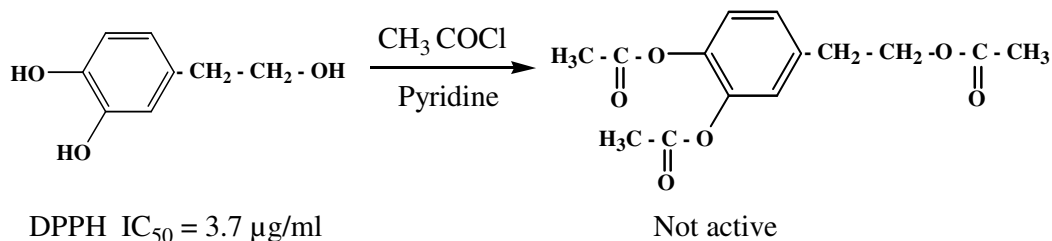
pp 9230–9237

Satoshi Obika\*, S. M. Abdur Rahman, Bingbing Song, Mayumi Onoda, Makoto Koizumi, Koji Morita, Takeshi Imanishi

**Synthesis and recovery of high bioactive phenolics from table-olive brine process wastewater**

pp 9238–9246

Mohamed Bouaziz\*, Saloua Lassoued, Zouhaier Bouallagui, Sana Smaoui, Adel Gargoubi, Abdelhafid Dhouib, Sami Sayadi

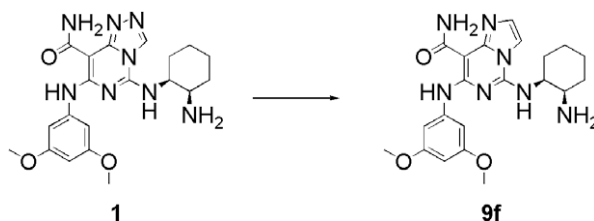


Hydroxytyrosol recovered from Meski cultivar table-olive wastewater processing and its synthesized acetyl analogue, triacetylhydroxytyrosol, were tested for their biological activities.

**Structure–activity relationship studies of imidazo[1,2-*c*]pyrimidine derivatives as potent and orally effective Syk family kinases inhibitors**

pp 9247–9260

Akihito Hirabayashi\*, Harunobu Mukaiyama, Hiroaki Kobayashi, Hiroaki Shiohara, Satoko Nakayama, Motoyasu Ozawa, Eiichi Tsuji, Keiji Miyazawa, Keiko Misawa, Hideki Ohnota, Masayuki Isaji

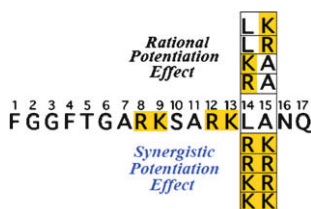


The conversion of 1,2,4-triazolo[4,3-*c*]pyrimidine to a imidazo[1,2-*c*]pyrimidine derivative improves in vivo efficacy of suppression of both passive cutaneous anaphylaxis (PCA) reaction and ConA-induced IL-2 production. Additionally, the inhibitory effects of the derivatives on Syk family kinase activity were assessed.

**Synergistic effect of basic residues at positions 14–15 of nociceptin on binding affinity and receptor activation**

pp 9261–9267

Kazushi Okada, Kaname Isozaki, Jinglan Li, Ayami Matsushima, Takeru Nose, Tommaso Costa, Yasuyuki Shimohigashi\*

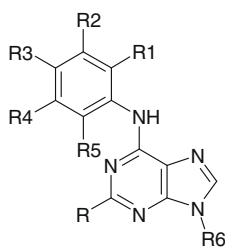


[Arg-Lys14-15]nociceptin is a superagonist of the ORL1 receptor. We clarified that the synergistic potentiation occurs only when basic amino acids are simultaneously incorporated.

**Novel potent inhibitors of *A. thaliana* cytokinin oxidase/dehydrogenase**

pp 9268–9275

Marek Zatloukal, Markéta Gemrotová, Karel Doležal\*, Libor Havlíček, Lukáš Spíchal, Miroslav Strnad

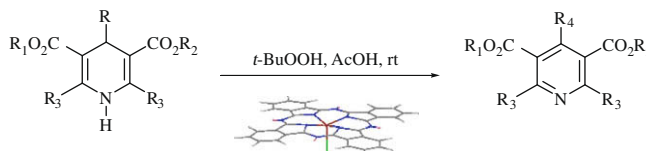


The synthesis of a new group of 6-anilinopurines, including compounds with potential cytokinin oxidase/dehydrogenase AtCKX2 inhibitory activity, is described.


**A highly efficient biomimetic aromatization of Hantzsch-1,4-dihydropyridines with *t*-butylhydroperoxide, catalysed by iron(III) phthalocyanine chloride**

pp 9276–9282

Mirela Filipan-Litvić, Mladen Litvić\*, Vladimir Vinković

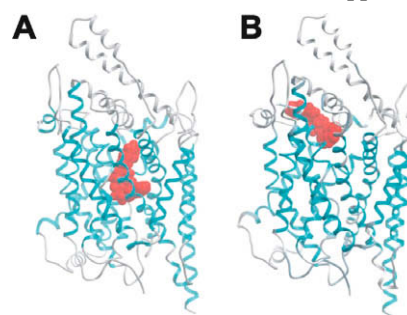


Rapid aromatization of Hantzsch-1,4-DHPs with *t*-butyl-hydroperoxide catalysed by iron(III) phthalocyanine chloride is described. The reaction proceeds smoothly at room temperature within 1–35 min and the products of high purity were isolated in excellent yields (88–99%).

**The molecular interactions of buspirone analogues with the serotonin transporter**

Małgorzata Jarończyk, Zdzisław Chilmonczyk, Aleksander P. Mazurek, Gabriel Nowak, Aina W. Ravna, Kurt Kristiansen, Ingebrigt Sylte\*

pp 9283–9294

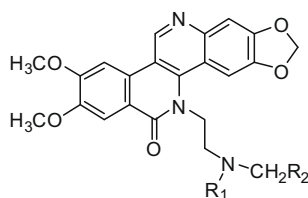


Ligand-binding sites of buspirone analogues (indicated in red) in the 3D model of SERT based on the LeuT<sub>AA</sub> X-ray crystal structure. (A) A putative high-affinity binding site. (B) A putative low-affinity binding site.

**Synthesis of N-substituted 5-[2-(N-alkylamino)ethyl]dibenzo[c,h][1,6]naphthyridines as novel topoisomerase I-targeting antitumor agents**

pp 9295–9301

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



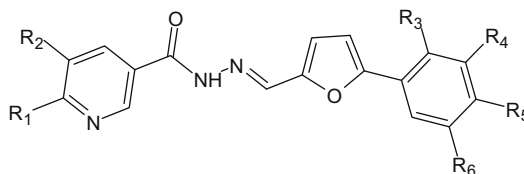
R1 = methyl, ethyl, isopropyl

R2 = cyano, trifluoromethyl, ethynyl, aminocarbonyl

**Computational structure–activity relationship analysis of non-peptide inducers of macrophage tumor necrosis factor- $\alpha$  production**

pp 9302–9312

Andrei I. Khlebnikov\*, Igor A. Schepetkin, Liliya N. Kirpotina, Mark T. Quinn\*

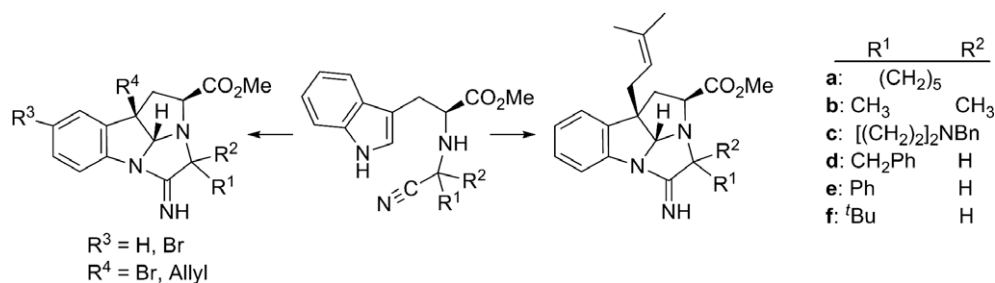


SAR analysis of 86 arylcarboxylic acid hydrazides using atom pair descriptors defines key molecular features important for these compounds to induce macrophage TNF- $\alpha$  production.

**Synthesis and antitumoral evaluation of indole alkaloid analogues containing an hexahydropyrrolo[1',2',3':1,9a,9]imidazo[1,2-a]indole skeleton**

pp 9313–9322

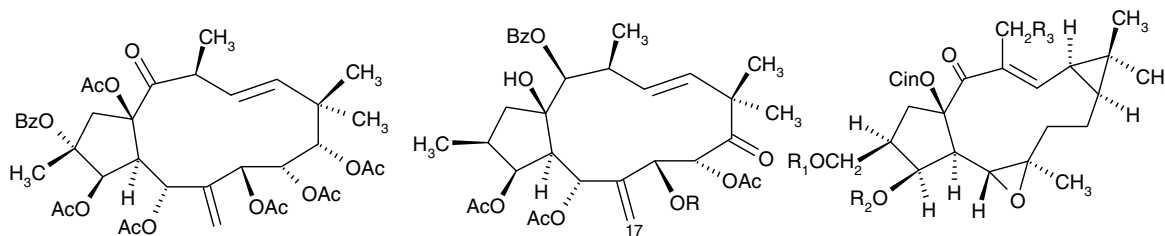
Pilar Ventosa-Andrés, Juan A. González-Vera, Ángel M. Valdivielso, M. Teresa García-López, Rosario Herranz\*



**Synergistic interaction between p-glycoprotein modulators and epirubicine on resistant cancer cells**

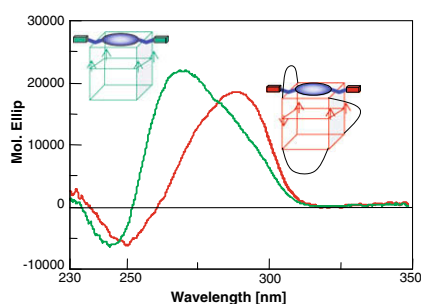
pp 9323–9330

Noélia Duarte, Anett Járđánházy, Joseph Molnár, Andreas Hilgeroth, Maria-José U. Ferreira \*

**Perylene side chains modulate G-quadruplex conformation in biologically relevant DNA sequences**

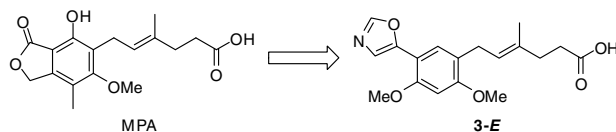
pp 9331–9339

Claudia Pivetta, Lorena Lucatello, A. Paul Krapcho, Barbara Gatto, Manlio Palumbo, Claudia Sissi \*

**Mycophenolic acid analogs with a modified metabolic profile**

pp 9340–9345

Liqiang Chen\*, Daniel J. Wilson, Nicholas P. Labello, Hiremagalur N. Jayaram, Krzysztof W. Pankiewicz

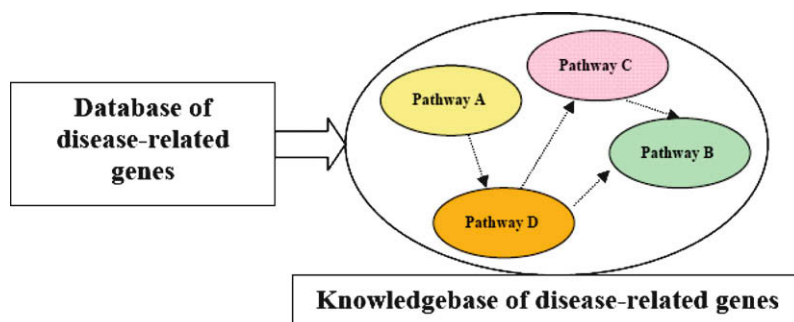


Aiming to circumvent the metabolic liability imposed by mycophenolic acid (MPA), a series of MPA analogs have been designed by combining the structural elements of MPA and known IMPDH inhibitors.

**Knowledgebase for addiction-related genes: Is it possible an extrapolation to rational multi-target drug design?**

pp 9346–9348

L. Michel Espinoza-Fonseca

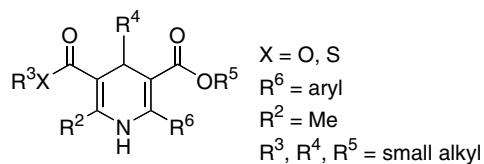




**Structure–activity relationships of 1,4-dihydropyridines that act as enhancers of the vanilloid receptor 1 (TRPV1)**

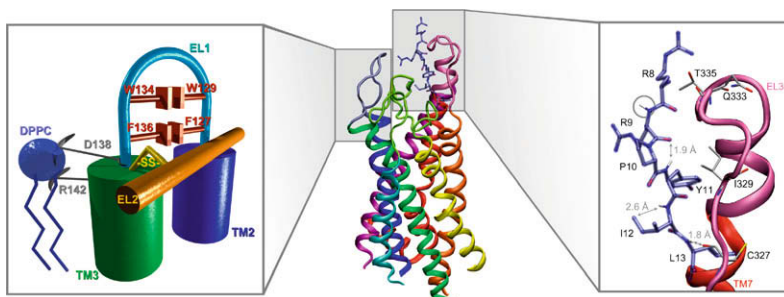
pp 9349–9358

Eun Joo Roh, Jason M. Keller, Zoltan Olah, Michael J. Iadarola\*, Kenneth A. Jacobson\*

**Novel insights into GPCR–Peptide interactions: Mutations in extracellular loop 1, ligand backbone methylations and molecular modeling of neurotensin receptor 1**

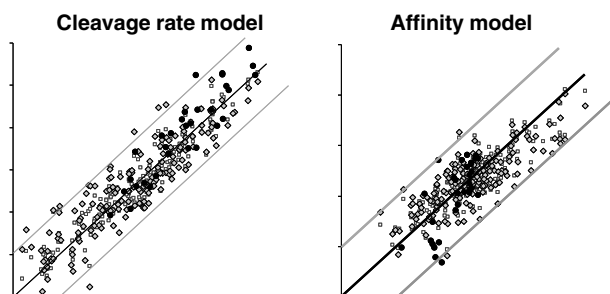
pp 9359–9368

Steffen Härterich, Susanne Koschatzky, Jürgen Einsiedel, Peter Gmeiner\*

**Proteochemometrics analysis of substrate interactions with dengue virus NS3 proteases**

pp 9369–9377

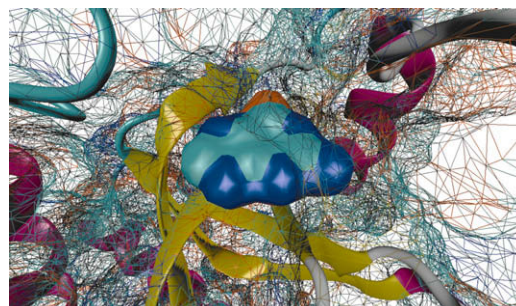
Peteris Prusis, Maris Lapins, Sviatlana Yahorava, Ramona Petrovska, Pornwaratt Niyomrattanakit, Gerd Katzenmeier, Jarl E. S. Wikberg\*

**Evaluation of ligand-binding affinity using polynomial empirical scoring functions**

pp 9378–9382

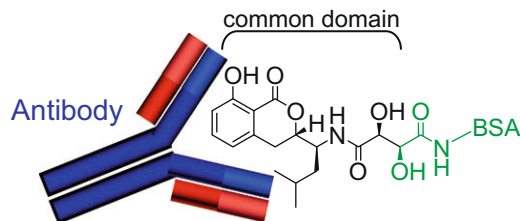
Walter Filgueira de Azevedo Jr.,\* Raquel Dias

We describe here the use of a new set of empirical scoring functions to assess ligand-binding affinities. This figure illustrates one of the complex used in the test set.



**Original preparation of conjugates for antibody production against Amicoumacin-related anti-microbial agents****pp 9383–9391**


Svitlana Shinkaruk, Bernard Bennetau\*, Pierre Babin, Jean-Marie Schmitter,  
Valerie Lamothe, Catherine Bennetau-Pelissero, Maria C. Urdaci\*



Specific recognition of the common domain of the Amicoumacin family.

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\*Corresponding author

 Supplementary data available via ScienceDirect

**COVER**

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (<http://www.pymol.org>). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, 102, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, 61(6), 355–360].

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