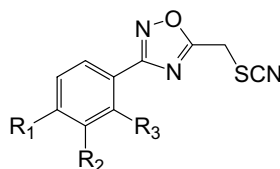


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Antikinetoplastid activity of 3-aryl-5-thiocyanatomethyl-1,2,4-oxadiazoles

pp 2815–2824

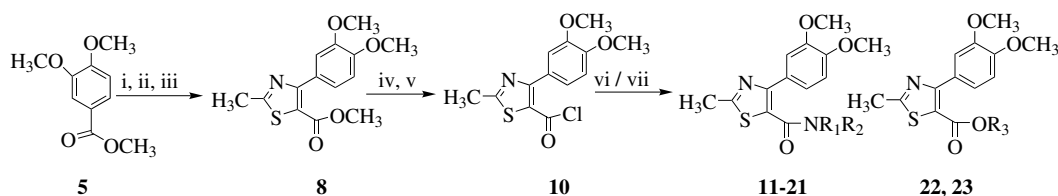
 Denise M. Cottrell, Jeffrey Capers, Manar M. Salem, Kate DeLuca-Fradley,
 Simon L. Croft and Karl A. Werbovetz*


A series of 3-aryl-5-thiocyanatomethyl-1,2,4-oxadiazoles was synthesized and tested for activity against *Leishmania* and African trypanosomes. Compounds **4b** ($R_1 = \text{Cl}$, $R_2 = R_3 = \text{H}$) and **4h** ($R_1 = R_2 = \text{Cl}$, $R_3 = \text{H}$) were the most active in vitro, displaying IC_{50} values of 4.5 and 2.3 μM against *L. donovani* amastigote-like forms, respectively. Compound **4b** reduced liver parasite burdens in a murine model of visceral leishmaniasis by 61% at an oral dose of 50 mg/kg/day for 5 days.

Design, synthesis, and biological activity of novel 4-(3,4-dimethoxyphenyl)-2-methylthiazole-5-carboxylic acid derivatives

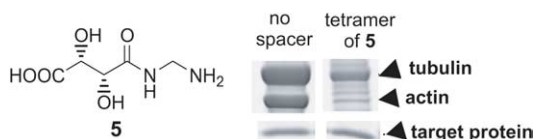
pp 2825–2830

Chang-Ling Liu,* Lin Li and Zheng-Ming Li


Design and synthesis of novel hydrophilic spacers for the reduction of nonspecific binding proteins on affinity resins

pp 2831–2841

Takaaki Shiyama, Minoru Furuya, Akira Yamazaki, Tomohiro Terada and Akito Tanaka*

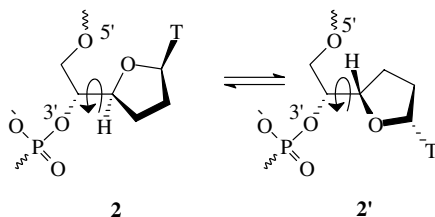


Tubulin and actin often bind nonspecifically to affinity chromatography resins, complicating research toward identifying the cellular targets of small molecules. We herein disclose the design, synthesis, and effectiveness in reduction of nonspecific binding proteins, of novel hydrophilic spacers. Among them, a tartaric acid derivative **5** exhibited effective activity on reduction of the nonspecific binding proteins. Introduction of tetramer of **5** on TOYOPEARL resulted in reduction of 65% and 90% of tubulin and actin, respectively, while maintaining effective binding of the target protein.

Hexofuranosyl thymidines inserted into oligodeoxynucleotides via their two exocyclic hydroxy groups. pp 2843–2851

Oligo synthesis and RNase H activity

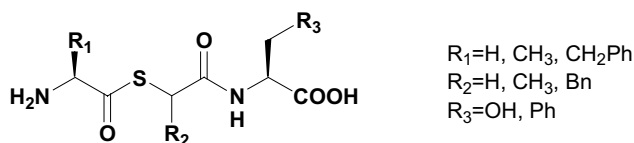
Vyacheslav V. Filichev, Birte Vester and Erik B. Pedersen*



A new type of nucleosides is considered as an acyclic nucleoside, which is conformationally restricted by a linking furanose ring. Thermal stability of its oligonucleotides with DNA/RNA complements and RNase H activity were studied.

Design and synthesis of chromogenic thiopeptolide substrates as MetAPs active site probes pp 2853–2861

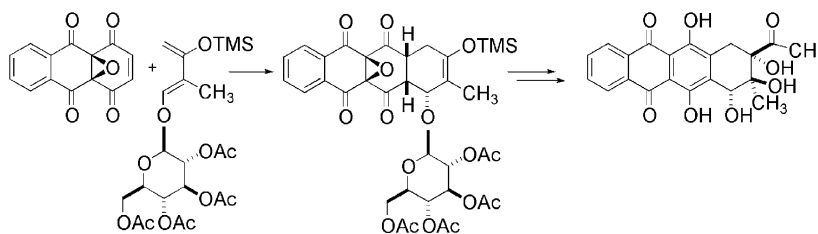
Yong-Mei Cui, Jing-Ya Li, Ling-Ling Chen, Jia Li, Qi-Zhuang Ye* and Fa-Jun Nan*



21 Chromogenic thiopeptolide substrates

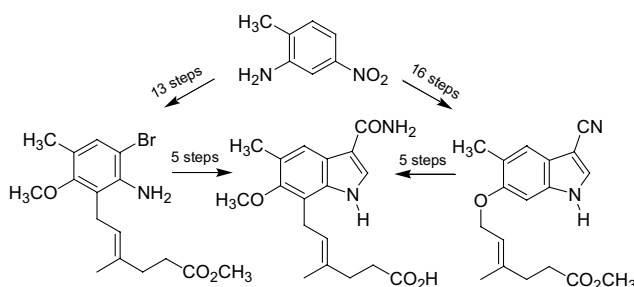
Enantioselective synthesis of (+)-8-hydroxy-8-methylidarubicinone pp 2863–2866

Laurance M. S. Bourghli* and R. J. Stoodley



Synthesis, molecular modeling, and evaluation of nonphenolic indole analogs of mycophenolic acid pp 2867–2879

Moustafa E. El-Araby,* Ralph J. Bernacki, Gergely M. Makara, Paula J. Pera and Wayne K. Anderson*



Platelet aggregation and antibacterial effects of an L-amino acid oxidase purified from *Bothrops alternatus* snake venom

pp 2881–2886

Rodrigo G. Stábeli, Silvana Marcussi, Guilherme B. Carlos, Rosemeire C. L. R. Pietro, Heloísa S. Selistre-de-Araújo, José R. Giglio, Eduardo B. Oliveira and Andreimar M. Soares*

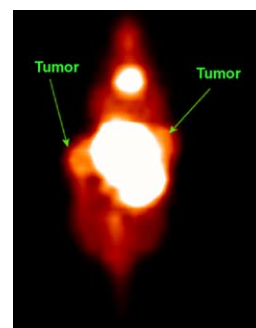
N-terminal sequence is: A D V R N P L E E F R E T D Y E V L

The present investigation reports the isolation and biochemical characterization of an L-amino acid oxidase (Balt-LAAO-I) from *Bothrops alternatus* venom, with special reference to its platelet aggregation effect and bactericidal activity.

[¹¹C]Choline as a PET biomarker for assessment of prostate cancer tumor models

pp 2887–2893

Qi-Huang Zheng,* Thomas A. Gardner, Sudhanshu Raikwar, Chinghai Kao, K. Lee Stone, Tanya D. Martinez, Bruce H. Mock, Xiangshu Fei, Ji-Quan Wang and Gary D. Hutchins

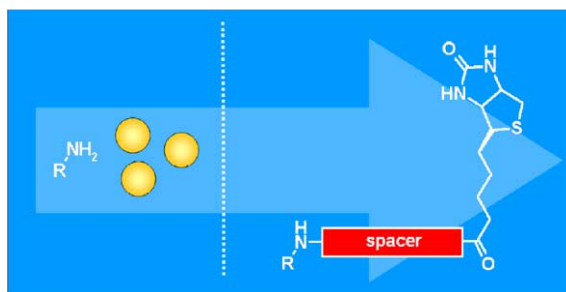


In vivo evaluation including biodistribution and micro-PET (positron emission tomography) imaging studies of [¹¹C]choline as a PET biomarker in four established human prostate cancer tumor models C4-2, PC-3, CWR22rv, and LNCaP tumor-bearing athymic mice is reported.

Polymer-bound reagents for the introduction of spacer-modified biotin labels

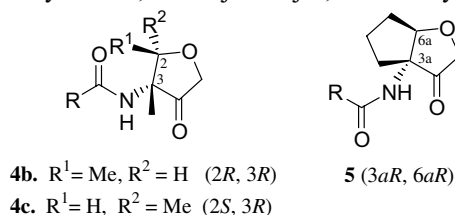
pp 2895–2902

Claudia Herforth, Philipp Heidler, Stephan Franke and Andreas Link*

**Functionalised 2,3-dimethyl-3-aminotetrahydrofuran-4-one and N-(3-oxo-hexahydrocyclopenta[b]-furan-3a-yl)acylamide based scaffolds: synthesis and cysteinyl proteinase inhibition**

pp 2903–2925

John Watts, Alex Benn, Nick Flinn, Tracy Monk, Manoj Ramjee, Peter Ray, Yikang Wang and Martin Quibell*

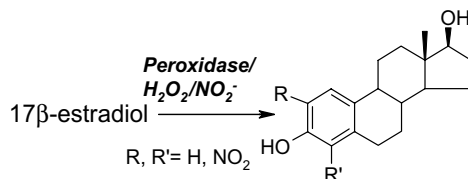


Fmoc-protected mono- and bicyclic α -alkylated ketones **4b**, **4c** and **5** were prepared through the corresponding diazomethylketone intermediates via a lithium chloride/acetic acid promoted insertion reaction. Building blocks **4b**, **4c** and **5** were utilised in a solid-phase synthesis of peptidomimetic inhibitors of a range of CAC1 cysteinyl proteinases.

17 β -Estradiol nitration by peroxidase/H₂O₂/NO₂⁻: a chemical assessment

pp 2927–2936

Alessandro Pezzella, Paola Manini, Paola Di Donato, Raffaele Boni, Alessandra Napolitano, Anna Palumbo and Marco d'Ischia*

**Modeling and interactions of *Aspergillus fumigatus* lanosterol 14- α demethylase 'A' with azole antifungals**

pp 2937–2950

Reena Gollapudy, Subhash Ajmani and Sudhir A. Kulkarni*



A homology model of AF-CYP51A built using MT-CYP51A as a template is described. This model was used to dock known azole antifungals such as fluconazole into the active site.

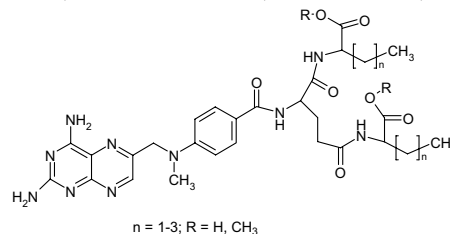
**Lipophilic conjugates of methotrexate with short-chain alkylamino acids as DHFR inhibitors. Synthesis, biological evaluation, and molecular modeling**

pp 2951–2964

Rosario Pignatello,* Salvatore Guccione, Stefano Forte, Claudia Di Giacomo, Valeria Sorrenti, Luisa Vicari, Gloria Uccello Barretta, Federica Balzano and Giovanni Puglisi

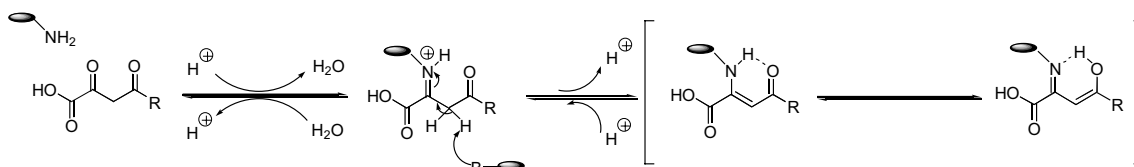
A new series of lipophilic α,γ -bis(amide) conjugates of the anticancer drug methotrexate (MTX) with short-chain 2-alkylamino acids (4–6 carbon atoms) was described.

The aim of these derivatives was to increase the uptake of the drug into transport-resistant tumor cell lines toward the uptake of MTX. The inhibitory activity of these compounds against the target enzyme, dihydrofolate reductase (DHFR), and a sensitive (CCRF-CEM) and a transport-resistant tumor cell subline (CEM-MTX) was assessed. The α,γ -bis(hexyl) derivative was the most active term of the series, showing the ability of retaining the same inhibitory activity also against the resistant cell subline, against which the parent drug was much less active than against the wild one. Docking studies combined with a conformational NMR analysis of MTX conjugates in solution are in agreement with the experimental biological data and the proposed binding mode.

**Slow-binding inhibition of 2-keto-3-deoxy-6-phosphogluconate (KDPG) aldolase**

pp 2965–2972

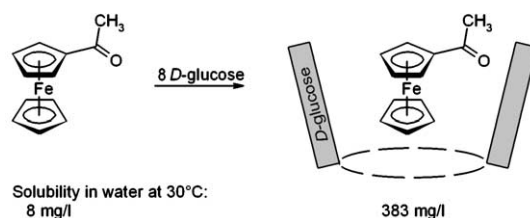
Rémi Braga, Laurence Hecquet and Casimir Blonski*



Saccharides as efficacious solubilisers for highly lipophilic compounds in aqueous media

pp 2973–2983

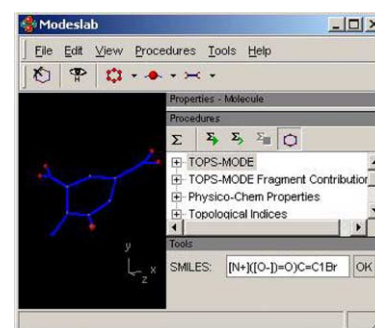
Martin Bertau* and Gerhard Jörg

**A TOPS-MODE approach to predict affinity for A₁ adenosine receptors. 2-(Arylamino)adenosine analogues**

pp 2985–2993

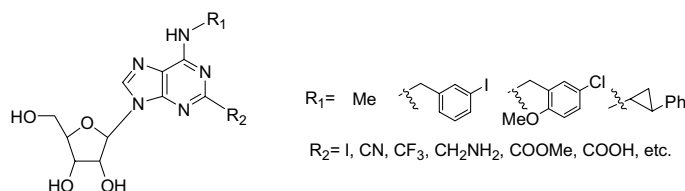
Maykel Pérez González* and Maria del Carmen Terán Moldes

The TOPological Sub-Structural Molecular Design (TOPS-MODE) approach has been applied to the study of the A₁ adenosine receptors. A model able to describe closed to 79% of the variance in the values for binding experiments of 32 analogues of these compounds was developed with the use of the mentioned approach.

**Modulation of adenosine receptor affinity and intrinsic efficacy in adenine nucleosides substituted at the 2-position**

pp 2995–3007

Michihiro Ohno, Zhan-Guo Gao, Philippe Van Rompaey, Susanna Tchilibon, Soo-Kyung Kim, Brian A. Harris, Ariel S. Gross, Heng T. Duong, Serge Van Calenbergh and Kenneth A. Jacobson*



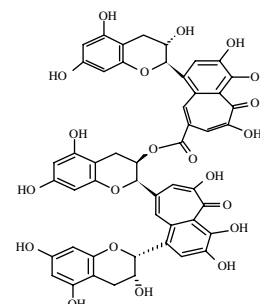
We have studied the structural determinants of binding affinity and efficacy of adenosine receptor (AR) agonists. Substituents at the 2-position of adenosine have been combined with N⁶-substitutions known to enhance human A₃AR affinity. The environment surrounding the 2-position within the putative A₃AR binding site was explored using rhodopsin-based homology modeling and ligand docking.

New dibenzotropolone derivatives characterized from black tea using LC/MS/MS

pp 3009–3017

Shengmin Sang,* Shiyong Tian, Ruth E. Stark, Chung S. Yang and Chi-Tang Ho

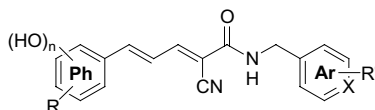
Three new dibenzotropolone, theadibenzotropolone **A**, **B** and **C**, together with one new tribenzotropolone, theatribenzotropolone **A** were formed by the reaction of theaflavins and tea catechins with horseradish peroxidase in the presence of H₂O₂. The structures of these new benzotropolone derivatives were elucidated on the basis of MS and 2D NMR spectroscopic analyses. The existence of these compounds in black tea was characterized by LC/ESI-MS/MS. Theadibenzotropolone **A** and **B** were the first benzotropolone-type trimers of catechins found in the black tea extract.



Tyrenes: synthesis of new antiproliferative compounds with an extended conjugation

pp 3019–3026

Peter Demin, Olga Rounova, Thomas Grunberger, Lorand Cimpean, Nigel Sharfe and Chaim M. Roifman*



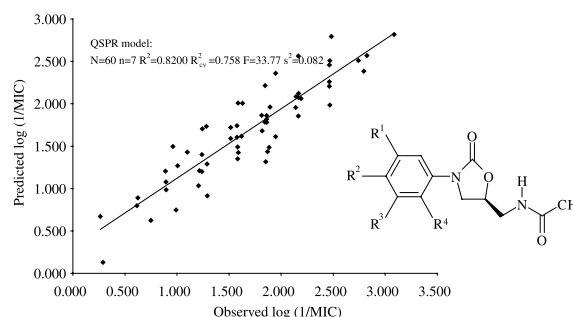
A series of substituted styryl-acrylonitriles was synthesized and tested for the ability to inhibit acute lymphocytic leukemia cancer cell growth. The compounds revealed great potency as antitumor agents.

QSPR of 3-aryloxazolidin-2-one antibacterials

pp 3027–3035

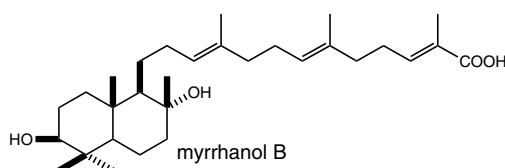
Alan R. Katritzky,* Dan C. Fara and Mati Karelson

A QSPR treatment has been applied to a data set consisting of 60 3-aryloxazolidin-2-one antibacterials to relate the in vitro minimum inhibitory concentration (MIC) (required for inhibiting growth of *Staphylococcus aureus*) with theoretical molecular and fragment descriptors. The treatment using CODESSA PRO descriptors leads to a seven-parameter model with $r^2 = 0.820$ and $r^2_{cv} = 0.758$.

**Absolute stereostructures of polypodane- and octanordammarane-type triterpenes with nitric oxide production inhibitory activity from guggul-gum resins**

pp 3037–3046

Hisashi Matsuda, Toshio Morikawa, Shin Ando, Hideo Oominami, Toshiyuki Murakami, Ikuko Kimura and Masayuki Yoshikawa*

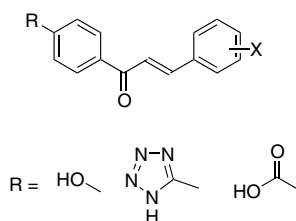


The MeOH ext. from guggul-gum resin was found to inhibit NO production in LPS-activated mouse peritoneal macrophages. From the MeOH ext., three new polypodane-type triterpenes, myrrhanol B and myrrhanones B and A acetate, and a new octanordammarane-type triterpene, epimansumbinol, were isolated. The several constituents showed inhibitory effects on NO production and iNOS induction.

Antibacterial chalcones—bioisosteric replacement of the 4'-hydroxy group

pp 3047–3054

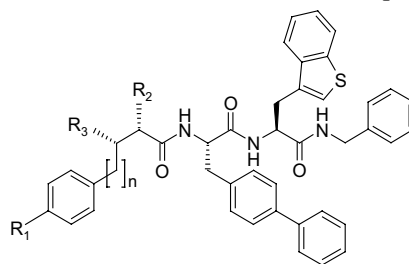
Simon Feldbæk Nielsen, Thomas Boesen, Mogens Larsen, Kristian Schønning and Hasse Kromann*



Small tripeptide surrogates with low nanomolar affinity as potent inhibitors of the botulinum neurotoxin B metallo-proteolytic activity

pp 3055–3062

Armand Blommaert, Serge Turcaud, Christine Anne and Bernard P. Roques*

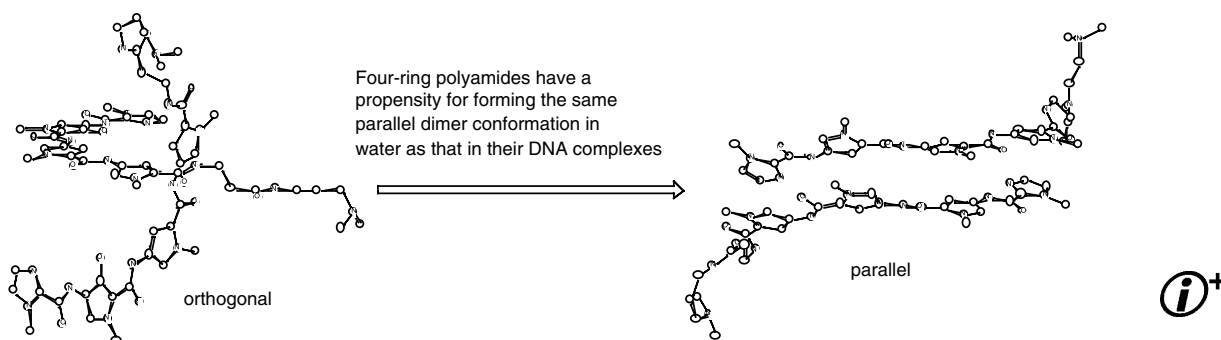


R₁₋₃ = various substituents,
n = 0 or 1

Nonbonded bivalence approach to cell-permeable molecules that target DNA sequences

pp 3063–3068

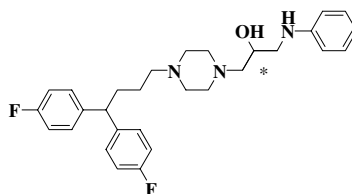
Yuan-Ping Pang*



Efficient asymmetric syntheses, determination of absolute configurations and biological activities of 1-[4,4-bis(4-fluorophenyl)butyl]-4-[2-hydroxy-3-(phenylamino)propyl]piperazine as a novel potent dopamine uptake inhibitor in the central nervous system

pp 3069–3078

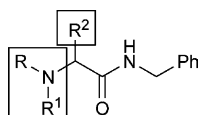
Makoto Kimura,* Tomoko Masuda, Koji Yamada, Masaki Mitani, Nobuo Kubota, Nobuyuki Kawakatsu, Kenichi Kishii, Masato Inazu, Yuji Kiuchi, Katsuji Oguchi and Takayuki Namiki*



N-Substituted amino acid N-benzylamides: synthesis, anticonvulsant, and metabolic activities

pp 3079–3096

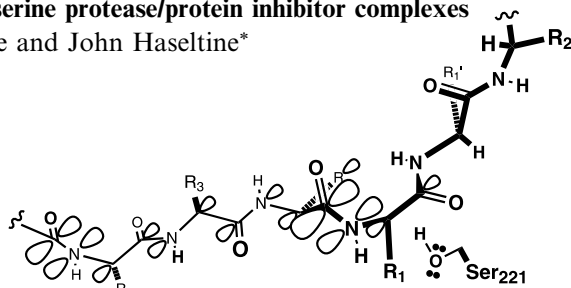
Cécile Béguin, Arnaud LeTiran, James P. Stables, Robert D. Voyksner and Harold Kohn*



Intramolecular orbital alignments in serine protease/protein inhibitor complexes

pp 3097–3106

Yun-Hua Fan, Claire-Anne Grégoire and John Haseltine*




An analysis of complexes between serine proteases and their protein inhibitors reveals extensive alignments of atomic orbitals in the bound strand and the active-serine-bearing strand. This implies that some kind of long-range backbone electronics are involved in the proteolytic mechanism.

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Instructions to contributors

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*Corresponding author

 Supplementary data available via ScienceDirect
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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