

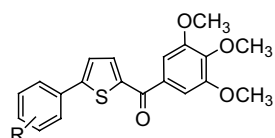
Contents

ARTICLES

Design, synthesis, and biological evaluation of thiophene analogues of chalcones

pp 5367–5376

Romeo Romagnoli,* Pier Giovanni Baraldi,* Maria Dora Carrion, Carlota Lopez Cara, Olga Cruz-Lopez, Delia Preti, Manlio Tolomeo, Stefania Grimaudo, Antonella Di Cristina, Nicola Zonta, Jan Balzarini, Andrea Brancale, Taradas Sarkar and Ernest Hamel

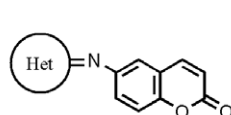


R = halogen, OCH₃, CH₃, NO₂

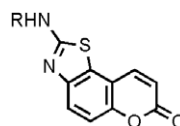
Synthesis and preliminary evaluation of some substituted coumarins as anticonvulsant agents

pp 5377–5388

Kamelia M. Amin, Doaa E. Abdel Rahman* and Yasmin A. Al-Eryani



Het = substituted thiazolidin-4-one, substituted thiazoline

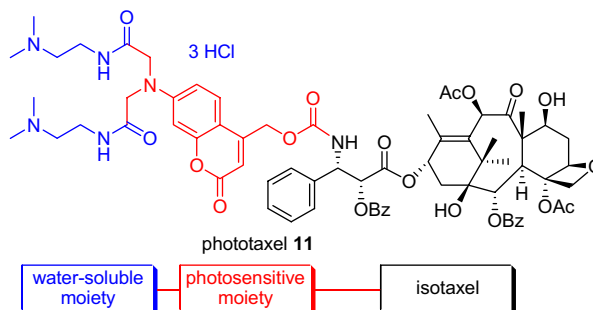


R = CH₃, C₂H₅, C₃H₇ and thiazolidin-4-one

Development of novel water-soluble photocleavable protective group and its application for design of photoresponsive paclitaxel prodrugs

pp 5389–5397

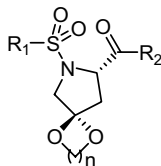
Mayo Noguchi, Mariusz Skwarczynski, Halan Prakash, Shun Hirota, Tooru Kimura, Yoshio Hayashi and Yoshiaki Kiso*



Design, synthesis and evaluation of novel sulfonyl pyrrolidine derivatives as matrix metalloproteinase inhibitors

pp 5398–5404

Xian-Chao Cheng, Qiang Wang, Hao Fang, Wei Tang and Wen-Fang Xu*

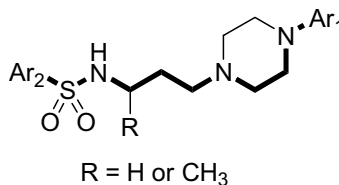


A series of novel sulfonyl pyrrolidine derivatives were designed, synthesized and assayed for their inhibitory activities on matrix metalloproteinase 2 (MMP-2) and aminopeptidase N (AP-N).

Preparation of piperazine derivatives as 5-HT₇ receptor antagonists

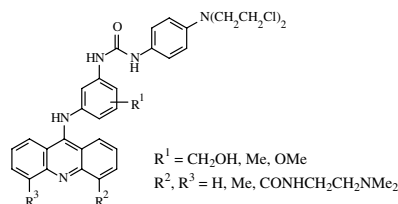
pp 5405–5412

Juhee Yoon, Eun A Yoo, Ji-Yeon Kim, Ae Nim Pae, Hyewhon Rhim, Woo-Kyu Park, Jae Yang Kong and Hea-Young Park Choo*


Synthesis and biological activity of stable and potent antitumor agents, aniline nitrogen mustards linked to 9-anilinoacridines via a urea linkage

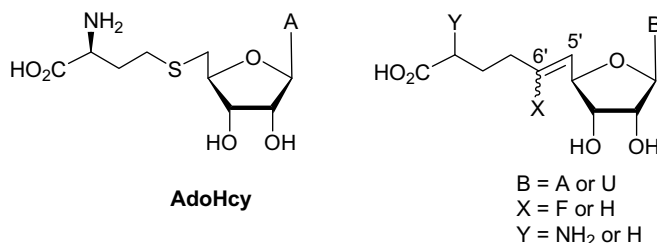
pp 5413–5423

Naval Kapuriya, Kalpana Kapuriya, Xiuguo Zhang, Ting-Chao Chou, Rajesh Kakadiya, Yu-Tse Wu, Tung-Hu Tsai, Yu-Ting Chen, Te-Chang Lee, Anamik Shah, Yogesh Naliapara and Tsann-Long Su*


Synthesis of 5'-functionalized nucleosides: S-Adenosylhomocysteine analogues with the carbon-5' and sulfur atoms replaced by a vinyl or halovinyl unit

pp 5424–5433

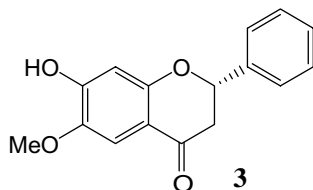
Stanislaw F. Wnuk,* Pablo R. Sacasa, Elzbieta Lewandowska, Daniela Andrei, Sumin Cai and Ronald T. Borchardt



Cytotoxic constituents from Brazilian red propolis and their structure–activity relationship

pp 5434–5440

Feng Li, Suresh Awale, Yasuhiro Tezuka and Shigetoshi Kadota*

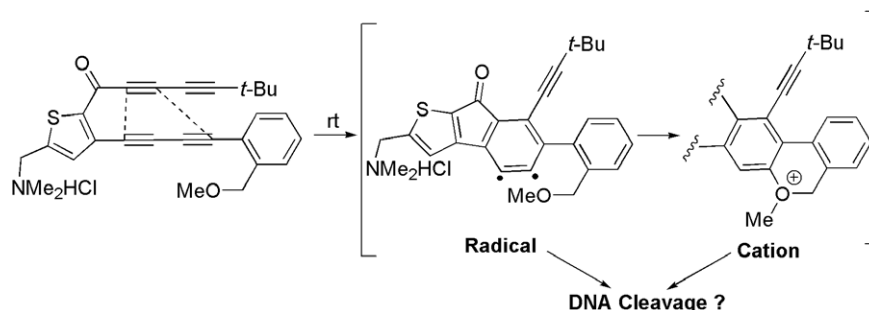


Colon 26-L5	B16-BL6	LLC	A549	HeLa	HT-1080
IC ₅₀ (μM)					
5.9	6.7	9.3	8.6	5.6	7.9

Synthesis and DNA cleaving activity of water-soluble non-conjugated thienyl tetraynes

pp 5441–5451

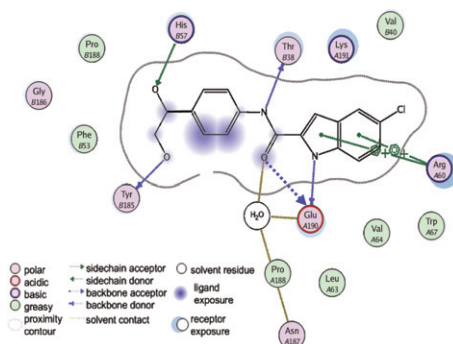
Kohei Torikai,* Yoichi Otsuka, Makoto Nishimura, Megumi Sumida, Tomoji Kawai, Kiyotoshi Sekiguchi and Ikuo Ueda

**Synthesis of 5-chloro-*N*-aryl-1*H*-indole-2-carboxamide derivatives as inhibitors of human liver glycogen phosphorylase *a***

pp 5452–5464

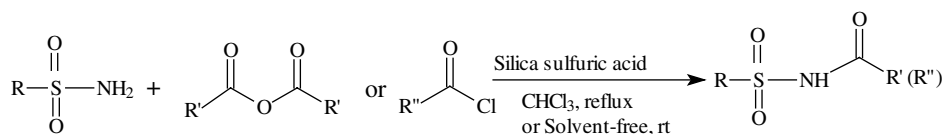
Kenichi Onda,* Takayuki Suzuki, Ryota Shiraki, Yasuhiro Yonetoku, Kenji Negoro, Kazuhiro Momose, Naoko Katayama, Masaya Orita, Tomohiko Yamaguchi, Mitsuaki Ohta and Shin-ichi Tsukamoto

5-Chloro-*N*-[4-(1,2-dihydroxyethyl)phenyl]-1*H*-indole-2-carboxamide and its pyridine analog are potent inhibitors of human liver glycogen phosphorylase *a* (hLGP_a) that binds in a solvent cavity at the hLGP_a dimer interface.

**Synthesis, in vitro antibacterial and carbonic anhydrase II inhibitory activities of *N*-acylsulfonamides using silica sulfuric acid as an efficient catalyst under both solvent-free and heterogeneous conditions**

pp 5465–5472

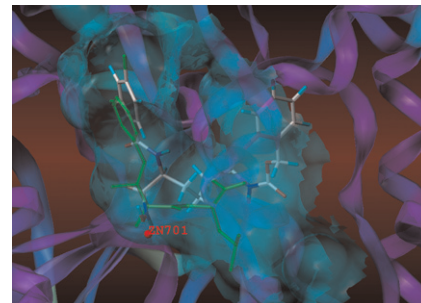
Ahmad Reza Massah,* Hadi Adibi,* Reza Khodarahmi, Ramin Abiri, Mohammad Bagher Majnooni, Sherita Shahidi, Beheshteh Asadi, Masomeh Mehrabi and Mohammad Ali Zolfigol



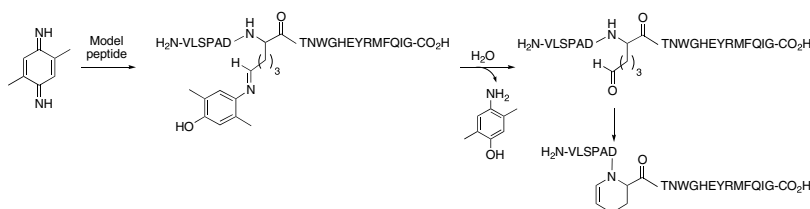
A series of *N*-acylsulfonamides was synthesized using silica sulfuric acid and evaluated for antibacterial activity against Gram-positive and Gram-negative microorganisms and also for inhibition of carbonic anhydrase II.

Design, synthesis, and QSAR studies of novel lysine derivatives as amino-peptidase N/CD13 inhibitors pp 5473–5481
 Qiang Wang, Maoying Chen, Huawei Zhu, Jie Zhang, Hao Fang, Binghe Wang and Wenfang Xu*

From the docking results and energy analysis, we found the pharmacophoric conformation of B6 (Bestatin in the X-ray crystal is showed in green).

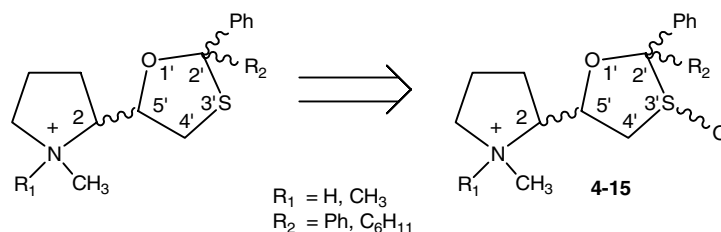


Sensitization to *p*-amino aromatic compounds: Study of the covalent binding of 2,5-dimethyl-*p*-benzoquinonediimine to a model peptide by electrospray ionization tandem mass spectrometry pp 5482–5489
 Joan Eilstein, Elena Giménez-Arnau, Daniel Duché, Nükhet Cavusoglu, Georges Hussler, Françoise Rousset and Jean-Pierre Lepoittevin*



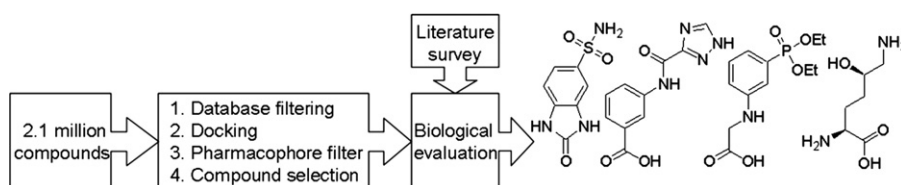
Lysine was an important amino acid when studying the hapten–protein complex formation of potentially allergenic *p*-benzoquinonediimines. Besides covalent binding, further degradation of lysine by oxidative deamination was observed.

Muscarinic antagonists with multiple stereocenters: Synthesis, affinity profile and functional activity of isomeric 1-methyl-2-(2,2-alkylaryl-1,3-oxathiolan-5-yl)pyrrolidine sulfoxide derivatives pp 5490–5500
 Silvia Dei,* Cristina Bellucci, Michela Buccioni, Marta Ferraroni, Luca Guandalini, Dina Manetti, Gabriella Marucci, Rosanna Matucci, Marta Nesi, Maria Novella Romanelli, Serena Scapecchi and Elisabetta Teodori



Evaluation of the amino acid binding site of *Mycobacterium tuberculosis* glutamine synthetase for drug discovery pp 5501–5513

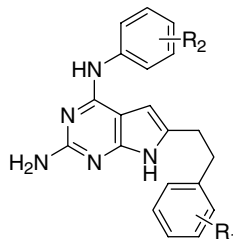
Anneli Nordqvist, Mikael T. Nilsson, Svenja Röttger, Luke R. Odell, Wojciech W. Krajewski, C. Evalena Andersson, Mats Larhed, Sherry L. Mowbray* and Anders Karlén*



Design, synthesis and biological evaluation of substituted pyrrolo[2,3-*d*]pyrimidines as multiple receptor tyrosine kinase inhibitors and antiangiogenic agents

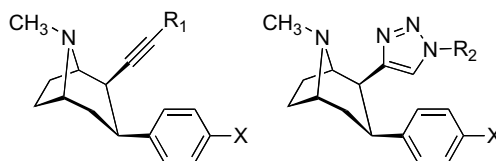
pp 5514–5528

Aleem Gangjee,* Ojas A. Namjoshi, Jianming Yu, Michael A. Ihnat, Jessica E. Thorpe and Linda A. Warnke

**Synthesis and receptor binding properties of 2 β -alkynyl and 2 β -(1,2,3-triazol)substituted 3 β -(substituted phenyl)tropane derivatives**

pp 5529–5535

Chunyang Jin, Hernán A. Navarro and F. Ivy Carroll*

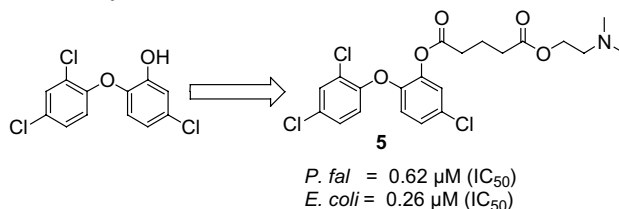


A series of novel 2 β -alkynyl and 2 β -(1,2,3-triazol)substituted 3 β -(substituted phenyl)tropane derivatives have been synthesized and evaluated for their monoamine transporter binding properties.

Design, synthesis, and application of novel triclosan prodrugs as potential antimalarial and antibacterial agents

pp 5536–5546

Satyendra Mishra, Krishanpal Karmodiya, Prasanna Parasuraman, Avadhesh Surolia* and Namita Surolia*

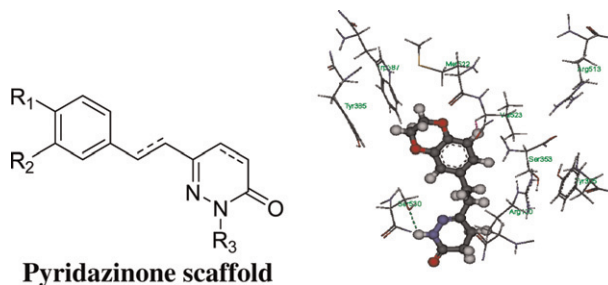


Novel triclosan-conjugated analogs bearing biodegradable ester linkage have been synthesized and evaluated for their antimalarial and antibacterial activities against *Plasmodium falciparum* and *Escherichia coli*. Many of the compounds were found to possess potent activities against *P. falciparum* and *E. coli* cultures.

Novel anti-inflammatory agents based on pyridazinone scaffold; design, synthesis and in vivo activity

pp 5547–5556

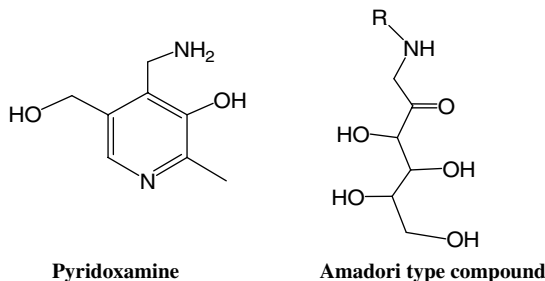
Khaled Abouzid* and Salma A. Bekhit



The pyridoxamine action on Amadori compounds: A reexamination of its scavenging capacity and chelating effect

pp 5557–5569

Miquel Adrover, Bartolomé Vilanova,* Juan Frau, Francisco Muñoz and Josefa Donoso



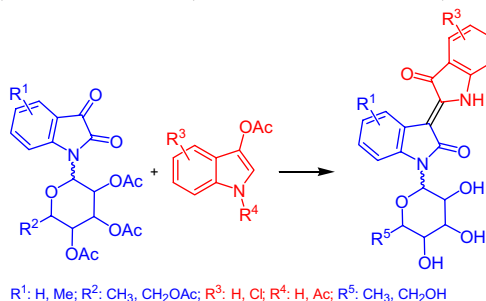
The blocking and chelating effect of pyridoxamine on Amadori type compounds have been analyzed in this work.



Synthesis of indirubin-*N'*-glycosides and their anti-proliferative activity against human cancer cell lines

pp 5570–5583

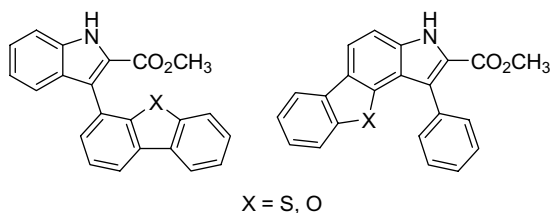
Stefanie Libnow, Karen Methling, Martin Hein, Dirk Michalik, Manuela Harms, Kristian Wende, Anke Flemming, Martin Köckerling, Helmut Reinke, Patrick J. Bednarski, Michael Lalk and Peter Langer*



Synthesis of new heteroaryl and heteroannulated indoles from dehydrophenylalanines: Antitumor evaluation

pp 5584–5589

Maria-João R. P. Queiroz,* Ana S. Abreu, M. Solange D. Carvalho, Paula M. T. Ferreira, Nair Nazareth and M. São-José Nascimento

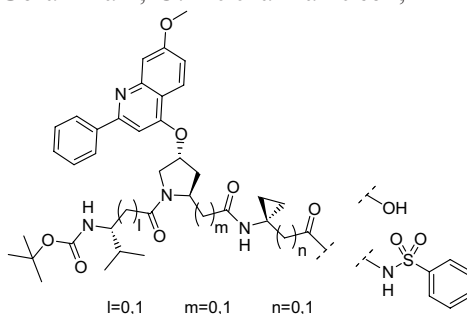


The growth inhibitory effect of three of the new compounds prepared was evaluated on the in vitro growth of three human tumor cell lines.

β -Amino acid substitutions and structure-based CoMFA modeling of hepatitis C virus NS3 protease inhibitors

pp 5590–5605

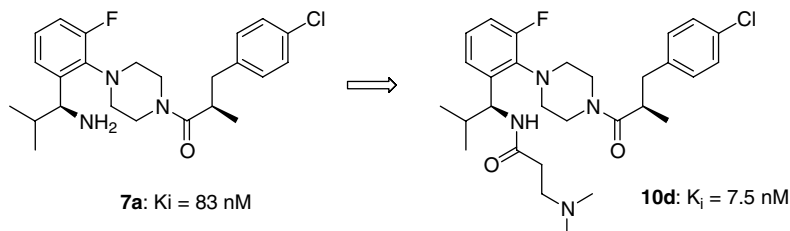
Johanna Nurbo, Shane D. Peterson, Göran Dahl, U. Helena Danielson, Anders Karlén and Anja Sandström*



Pharmacological and pharmacokinetic characterization of 2-piperazine- α -isopropyl benzylamine derivatives as melanocortin-4 receptor antagonists

pp 5606–5618

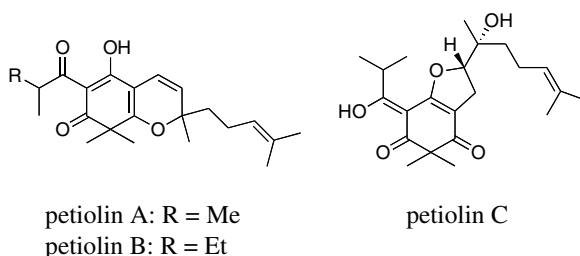
Chen Chen,* Fabio C. Tucci, Wanlong Jiang, Joe A. Tran, Beth A. Fleck, Sam R. Hoare, Jenny Wen, Takung Chen, Michael Johns, Stacy Markison, Alan C. Foster, Dragan Marinkovic, Caroline W. Chen, Melissa Arellano, John Harman, John Saunders, Haig Bozigian and Daniel Marks



Petiolins A–C, phloroglucinol derivatives from *Hypericum pseudopetiolum* var. *kiusianum*

pp 5619–5623

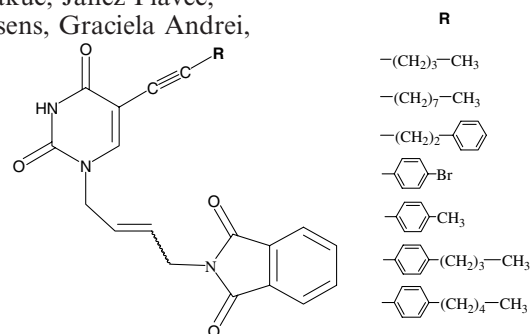
Naonobu Tanaka, Takaaki Kubota, Haruaki Ishiyama, Atsushi Araki, Yoshiki Kashiwada, Yoshihisa Takaishi, Yuzuru Mikami and Jun'ichi Kobayashi*



Synthesis, cytostatic and anti-HIV evaluations of the new unsaturated acyclic C-5 pyrimidine nucleoside analogues

pp 5624–5634

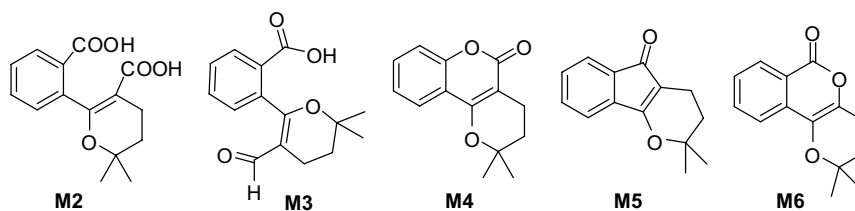
Tatjana Gazivoda, Silvana Raić-Malić, Vedran Krištafor, Damjan Makuc, Janez Plavec, Siniša Bratulić, Sandra Kraljević-Pavelić, Krešimir Pavelić, Lieve Naesens, Graciela Andrei, Robert Snoeck, Jan Balzarini and Mladen Mintas*



Synthetic methods for the preparation of ARQ 501 (β -Lapachone) human blood metabolites

pp 5635–5643

Rui-Yang Yang, Darin Kizer, Hui Wu, Erika Volckova, Xiu-Sheng Miao, Syed M. Ali, Manish Tandon, Ronald E. Savage, Thomas C. K. Chan and Mark A. Ashwell*

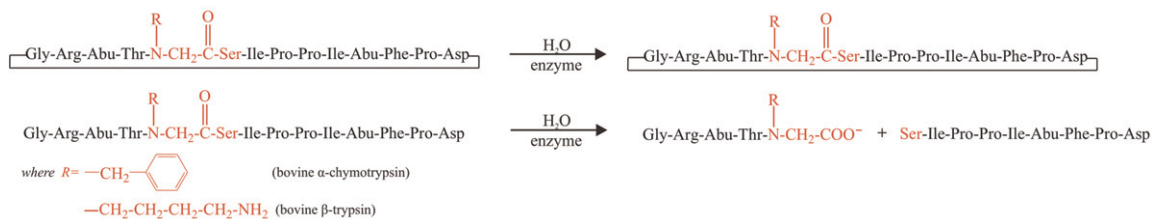


Synthesis of human blood metabolites (**M2–M6**) of ARQ 501 is described.

Peptomeric analogues of trypsin inhibitor SFTI-1 isolated from sunflower seeds

pp 5644–5652

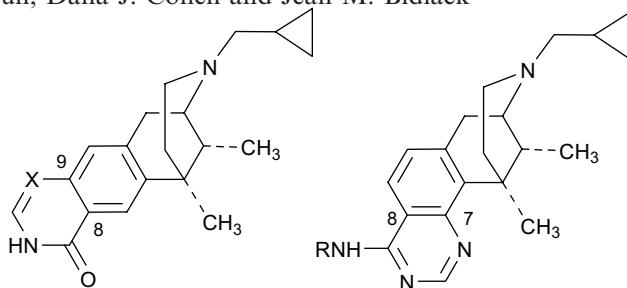
Anna Łęgowska,* Elżbieta Bulak, Magdalena Wysocka, Anna Jaśkiewicz,
Adam Lesner, Dawid Dębowski and Krzysztof Rolka



Redefining the structure–activity relationships of 2,6-methano-3-benzazocines. Part 6: Opioid receptor binding properties of cyclic variants of 8-carboxamidocyclazocine

pp 5653–5664

Mark P. Wentland,* Xufeng Sun, Dana J. Cohen and Jean M. Bidlack



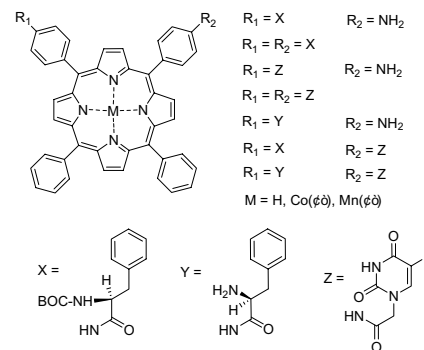
Novel 7,8- and 8,9-fused-heterocyclic variants of 8-carboxamidocyclazocine have high affinity for opioid receptors.

Synthesis and in vitro PDT activity of miscellaneous porphyrins with amino acid and uracil

pp 5665–5671

Shi Weimin, Zhang Gen, Dai Guifu, Zhang Yunxiao, Zhao Jin and Tao Jingchao*

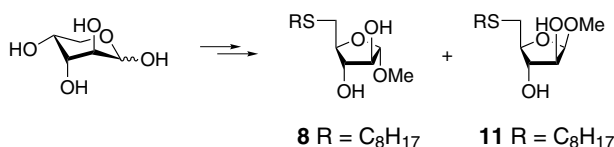
Miscellaneous porphyrins with L-phenylalanine and 5-Fu for photodynamic therapy.



Synthesis of methyl 5-S-alkyl-5-thio-D-arabinofuranosides and evaluation of their antimycobacterial activity

pp 5672–5682

Aditya K. Sanki, Julie Boucau, Parijat Srivastava, Samuel S. Adams,
Donald R. Ronning and Steven J. Sucheck*

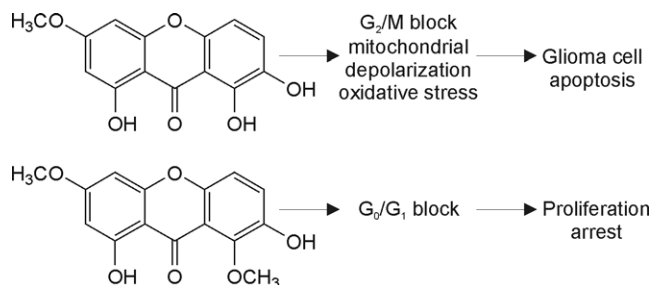


Methyl 5-S-alkyl-5-thio-D-arabinofuranosides were synthesized as potential inhibitors of mycobacterial antigen 85 complex. The most potent compounds **8** and **11** showed MICs of 256 and 512 $\mu\text{g/mL}$, respectively, against *Mycobacterium smegmatis* ATCC 14468.

Antiglioma action of xanthenes from *Gentiana kochiana*: Mechanistic and structure–activity requirements

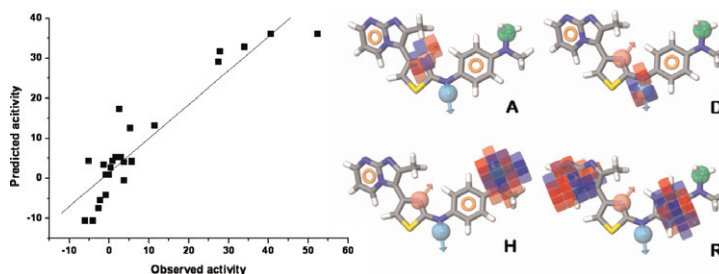
pp 5683–5694

Aleksandra Isakovic, Teodora Jankovic, Ljubica Harhaji, Sladjana Kostic-Rajacic, Zoran Nikolic, Vlatka Vajs and Vladimir Trajkovic*

**SAR and QSAR study on 2-aminothiazole derivatives, modulators of transcriptional repression in Huntington's disease**

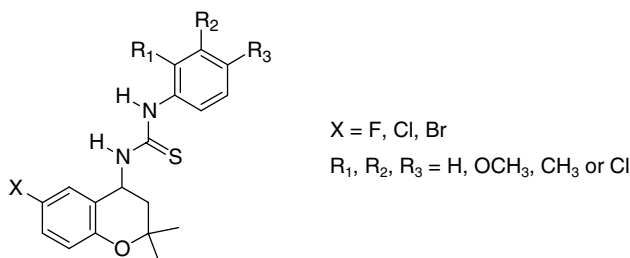
pp 5695–5703

Samantha Leone, Cesare Mutti, Aleksey Kazantsev, Mattia Sturlese, Stefano Moro, Elena Cattaneo, Dorotea Rigamonti* and Alessandro Contini*

**New *R/S*-3,4-dihydro-2,2-dimethyl-6-halo-4-(phenylaminothiocarbonylamino)-2*H*-1-benzopyrans structurally related to (±)-cromakalim as tissue-selective pancreatic β-cell K_{ATP} channel openers**

pp 5704–5719

Sophie Sebillé, Pascal de Tullio, Xavier Florence, Bénédicte Becker, Marie-Hélène Antoine, Catherine Michaux, Johan Wouters, Bernard Pirotte* and Philippe Lebrun

**Halogenated derivatives QSAR model using spectral moments to predict haloacetic acids (HAA) mutagenicity**

pp 5720–5732

Alfonso Pérez-Garrido,* Maykel Pérez González and Amalio Garrido Escudero*

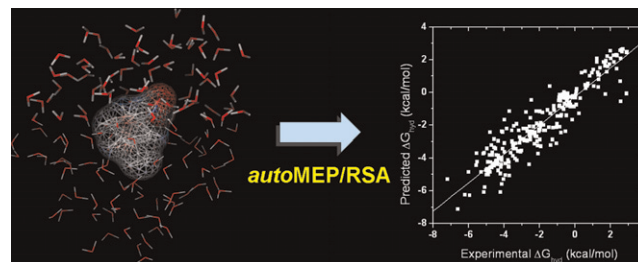


Prediction of the aqueous solvation free energy of organic compounds by using autocorrelation of molecular electrostatic potential surface properties combined with response surface analysis

pp 5733–5742

Lisa Michielan, Magdalena Bacilieri, Chosei Kaseda and Stefano Moro*

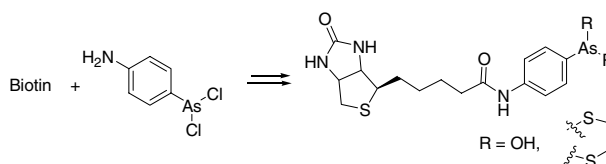
In the present study we have introduced *autocorrelation* molecular electrostatic potential (*autoMEP*) vectors in combination with nonlinear response surface analysis (RSA) as alternative 3D-QSPR strategy to evaluate the aqueous solvation free energy of organic compounds.



An improved synthesis of arsenic–biotin conjugates

pp 5743–5746

Jorge Heredia-Moya and Kenneth L. Kirk*



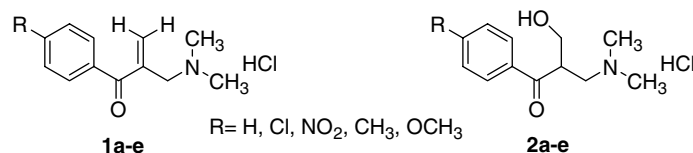
Biotin–arsenic conjugates are prepared conveniently and in good yield directly from *p*-aminophenyldichloroarsine and biotin.



1-Aryl-2-dimethylaminomethyl-2-propen-1-one hydrochlorides and related adducts: A quest for selective cytotoxicity for malignant cells

pp 5747–5753

Hari N. Pati, Umashankar Das, Masami Kawase, Hiroshi Sakagami, Jan Balzarini, Erik De Clercq and Jonathan R. Dimmock*

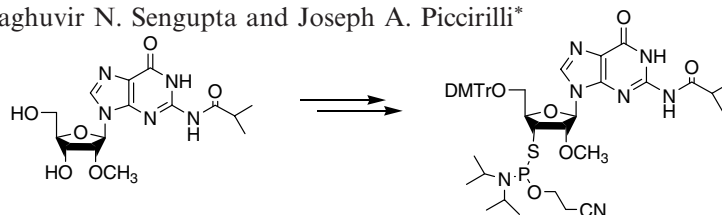


Representatives of series **1** and **2** demonstrated a disparity of cytotoxic potencies to tumor cells, preferential toxicity to neoplasms compared to normal cells, induced apoptosis and activated certain caspases.

Synthesis and biochemical application of 2'-*O*-methyl-3'-thioguanosine as a probe to explore group I intron catalysis

pp 5754–5760

Jun Lu, Nan-Sheng Li, Raghuvir N. Sengupta and Joseph A. Piccirilli*

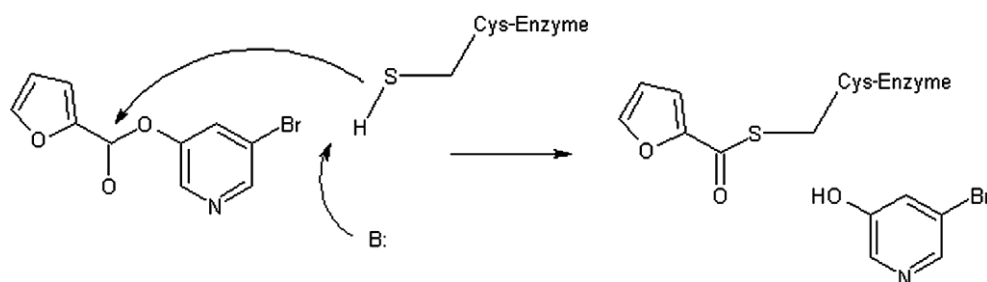


2'-*O*-Methyl-3'-thioguanosine phosphoramidite was synthesized in eight steps starting from 2'-*O*-methyl-*N*²-(isobutryl) guanosine with 10.4% overall yield. We have also utilized this analogue to investigate a potential hydrogen bond interaction in the *Tetrahymena* ribozyme reaction. Our results provide evidence against a model in which the guanosine nucleophile 3'-oxygen accepts a hydrogen bond from the adjacent 2'-hydroxyl group.

Heteroaromatic ester inhibitors of hepatitis A virus 3C proteinase: Evaluation of mode of action

pp 5761–5777

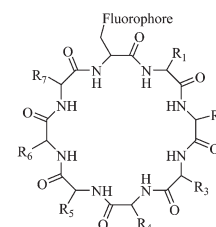
Carly Huitema, Jianmin Zhang, Jiang Yin, Michael N. G. James, John C. Vederas and Lindsay D. Eltis*

**Thermodynamics and fluorescence studies of the interactions of cyclooctapeptides with Hg^{2+} , Pb^{2+} , and Cd^{2+}**

pp 5778–5787

Maria Ngu-Schwemlein,* Willie Gilbert, Kshawna Askew and Stefanie Schwemlein

Isothermal titration calorimetry shows that CP1-3 bind Hg^{2+} and Pb^{2+} over Cd^{2+} . CP1-3 showed pronounced fluorescence quenching responses to Hg^{2+} . Fluorophore-tagged cyclooctapeptides may be useful as Hg^{2+} sensors.



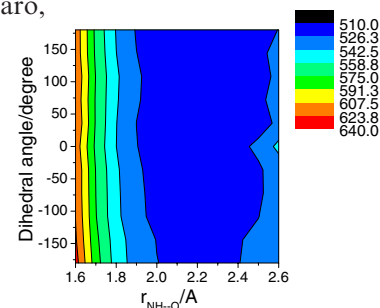
CP1: D-Glu-Glu-D-Glu-Glu-D-Leu-Leu-D-Leu-Trp
 CP2: Glu-D-Leu-Glu-D-Leu-Glu-D-Leu-Glu-D-Trp
 CP3: Glu-D-Leu-Cys-D-Leu-Glu-D-Leu-Cys-D-Trp

Sulfadiazine/hydroxypropyl- β -cyclodextrin host-guest system: Characterization, phase-solubility and molecular modeling

pp 5788–5794

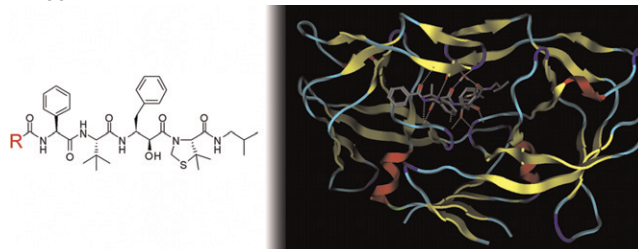
Márcia Valéria Gaspar de Araújo, Elze Kelly Barbosa Vieira, Gilderman Silva Lázaro, Leila Souza Conegero, Luís Eduardo Almeida, Ledjane Silva Barreto, Nivan Bezerra da Costa, Jr. and Iara F. Gimenez*

A 1:1 inclusion complex of sulfadiazine with hydroxypropyl β -cyclodextrin was prepared, characterized and modeled by RM1 and PM6 semiempirical methods. Phase-solubility and characterization of the system were carried out by standard methods.

**Synthesis and activity of tetrapeptidic HTLV-I protease inhibitors possessing different P_3 -cap moieties**

pp 5795–5802

Meihui Zhang, Jeffrey-Tri Nguyen, Henri-Obadja Kumada, Tooru Kimura, Maosheng Cheng, Yoshio Hayashi and Yoshiaki Kiso*



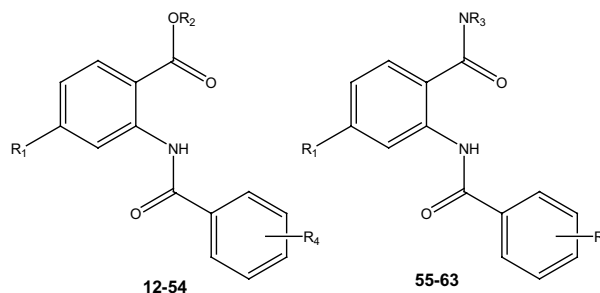
A series of novel tetrapeptidic HTLV-I protease inhibitors were prepared using an hydroxymethylcarbonyl isostere. Most inhibitors showed high HTLV-I and HIV-1 proteases inhibitory activity.

Synthesis and anti-platelet evaluation of 2-benzoylaminobenzoate analogs

pp 5803–5814

Pei-Wen Hsieh,* Shin-Zan Chiang, Chin-Chung Wu, Yi-Ching Lo, Yu-Tzu Shih and Yang-Chang Wu*

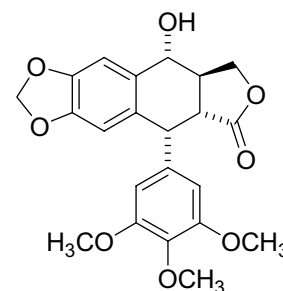
Fifty-two 2-benzoylaminobenzoate analogs were synthesized and subjected to anti-platelet aggregation assay. The results revealed that most of 2-benzoylaminobenzoic acid derivatives showed selectively inhibitory effect on AA-induced platelet aggregation.

**Podophyllotoxin directly binds a hinge domain in E2 of HPV and inhibits an E2/E7 interaction in vitro**

pp 5815–5825

Takeki Saitoh, Kouji Kuramochi, Takahiko Imai, Kei-ichi Takata, Masahide Takehara, Susumu Kobayashi, Kengo Sakaguchi and Fumio Sugawara*

In this report, we screened molecules binding to podophyllotoxin with T7 phage display clonings in order to obtain more information about molecular mechanism of the action. Thus, our results suggested that podophyllotoxin binds to a hinge domain of E2 in HPV and inhibited the E2/E7 interaction in vitro.

**OTHER CONTENTS****Instructions to contributors**

p I

*Corresponding author

i* 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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