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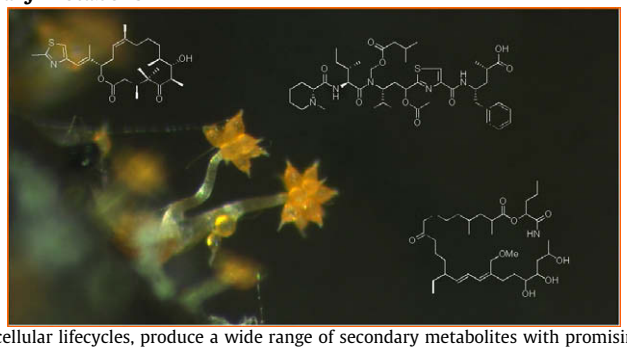
Bioorganic & Medicinal Chemistry Vol. 17, No. 6, 2009

Contents

Preface p 2120

SPECIAL ISSUE REVIEW

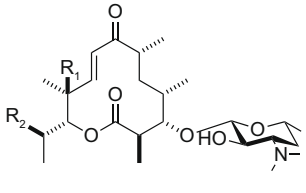
A brief tour of myxobacterial secondary metabolism pp 2121–2136
Kira J. Weissman, Rolf Müller *



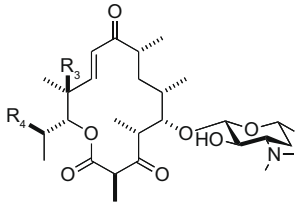
Myxobacteria nolable for their complex, multi-cellular lifecycles, produce a wide range of secondary metabolites with promising bioactivity.

SPECIAL ISSUE ARTICLES

The methymycin/pikromycin pathway: A model for metabolic diversity in natural product biosynthesis pp 2137–2146
Jeffrey D. Kittendorf, David H. Sherman *

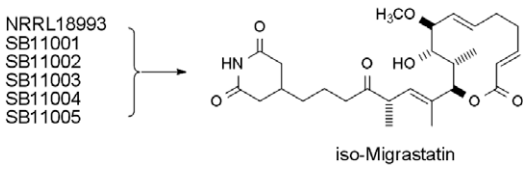


YC-17: R_1 = H, R_2 = H
methymycin: R_1 = OH, R_2 = H
neomethymycin: R_1 = H, R_2 = OH
novamethymycin: R_1 = OH, R_2 = OH



narbomycin: R_3 = H, R_4 = H
pikromycin: R_3 = OH, R_4 = H
neopikromycin: R_3 = H, R_4 = OH
novapikromcyin: R_3 = OH, R_4 = OH

Engineered production of *iso*-migrastatin in heterologous *Streptomyces* hosts pp 2147–2153
Zhiyang Feng, Liyan Wang, Scott R. Rajski, Zhinan Xu, Marie F. Coeffet-LeGal, Ben Shen *

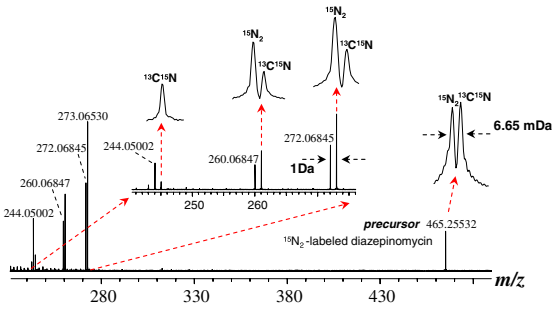


Production of *iso*-migrastatin in recombinant strains SB11001, SB11002, SB11003, SB11004, and SB11005 has been accomplished by BAC-mediated expression of the *iso*-migrastatin biosynthetic gene cluster from *Streptomyces platensis* NRRL18993 in five heterologous *Streptomyces* hosts.

Probing natural product biosynthetic pathways using Fourier transform ion cyclotron resonance mass spectrometry pp 2154–2161

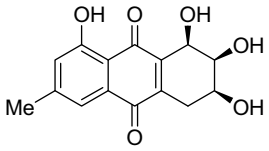
Xidong Feng*, Anokha S. Ratnayake, Romila D. Charan, Jeffrey E. Janso, Valerie S. Bernan, Gerhard Schlingmann, Haiyin He, Mark Tischler, Frank E. Koehn, Guy T. Carter *

FTMS/MS with ultra-high resolving power amplified the isotopic fine structure of the precursor ions from a few mDa to 1Da scale, making the assignment of $^{15}N_2$ labeling unequivocal.



Isolation, structure and antibacterial activity of pleosporone from a pleosporalean ascomycete discovered by using antisense strategy pp 2162–2166

Chaowei Zhang, John G. Ondeyka, Deborah L. Zink, Angela Basilio, Francisca Vicente, Javier Collado, Gonzalo Platas, Joann Huber, Karen Dorso, Mary Motyl, Kevin Byrne, Sheo B. Singh *

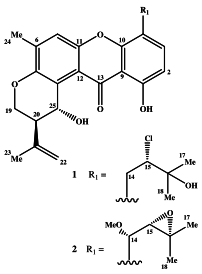


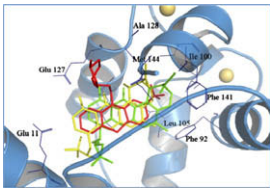
Isolation, structure, and biological activities of pleosporone are described.

Calmodulin inhibitors from the fungus *Emericella* sp. pp 2167–2174

Mario Figueroa, María del Carmen González, Rogelio Rodríguez-Sotres, Alejandro Sosa-Peinado, Martín González-Andrade, Carlos M. Cerda-García-Rojas, Rachel Mata *

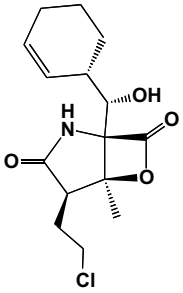
The new xanthones **1** and **2** were isolated from an extract of the mycelium and culture broth of *Emericella* sp. strain 25379 along with two known compounds. The structures of **1** and **2** were elucidated by spectroscopic and molecular modeling methods. The activation of the CaM-sensitive PDE1 was inhibited in the presence of all isolates. A docking analysis revealed that they interacted with CaM in the same pocket of TFP.





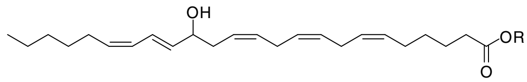
Discovery and development of the anticancer agent salinosporamide A (NPI-0052) pp 2175–2180

William Fenical, Paul R. Jensen, Michael A. Palladino, Kin S. Lam, G. Kenneth Lloyd, Barbara C. Potts *



A new antiangiogenic C_{24} oxylipin from the soft coral *Sinularia numerosa* pp 2181–2184

Takahiro Yamashita, Yoichi Nakao*, Shigeki Matsunaga, Tsutomu Oikawa, Yukimitsu Imahara, Nobuhiro Fusetani*

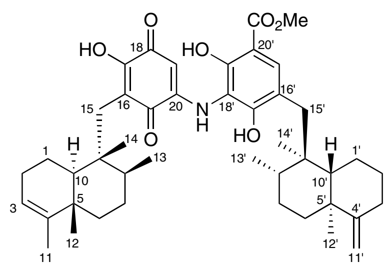


1: R = H 4: R = Me

A new antiangiogenic oxylipin, 15-hydroxy-tetracosa-6,9,12,16,18-pentaenoic acid (15-HTPE; **1**) was isolated as an inhibitor of tube formation from the soft coral *Sinularia numerosa*. Its structure was elucidated by means of spectral analysis and chemical degradation.

Nakijiquinones E and F, new dimeric sesquiterpenoid quinones from marine sponge pp 2185–2188

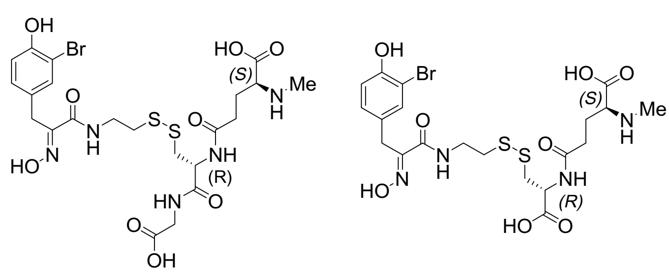
Yohei Takahashi, Takaaki Kubota, Jun'ichi Kobayashi*



nakijiquinone E (**1**)

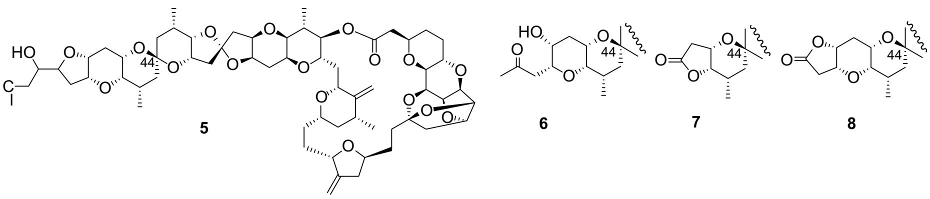
Psammaplin A as a general activator of cell-based signaling assays via HDAC inhibition and studies on some bromotyrosine derivatives pp 2189–2198

Malcolm W. B. McCulloch, Gary S. Coombs, Nikhil Banerjee, Tim S. Bugni, Kendell M. Cannon, Mary Kay Harper, Charles A. Veltri, David M. Virshup, Chris M. Ireland*



Antitumour polyether macrolides: Four new halichondrins from the New Zealand deep-water marine sponge *Lissodendoryx* sp. pp 2199–2203

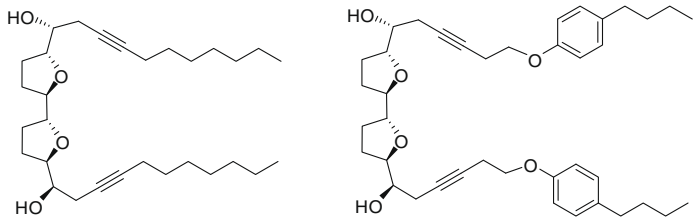
Sarah J. H. Hickford, John W. Blunt, Murray H. G. Munro*



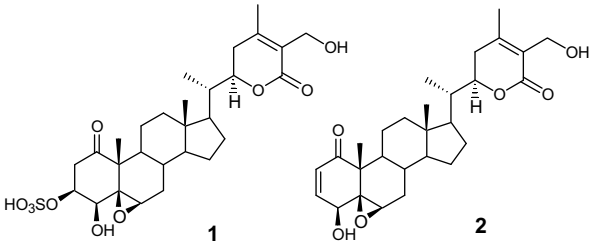
5 6 7 8

Four new potent antitumour halichondrins have been isolated from the marine sponge *Lissodendoryx* sp.

Synthesis and characterization of Δlac-acetogenins that potently inhibit mitochondrial complex I **pp 2204–2209**
Jean-Charles Chapuis, Omar Khdour, Xiaoqing Cai, Jun Lu, Sidney M. Hecht *

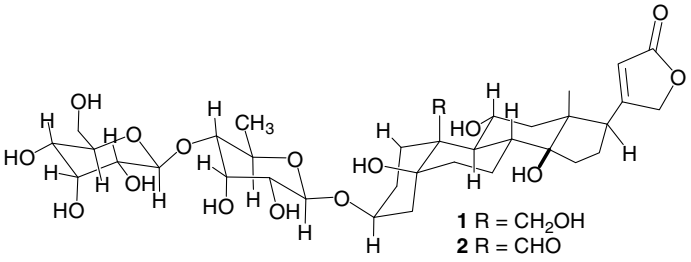


2,3-Dihydrowithaferin A-3β-*O*-sulfate, a new potential prodrug of withaferin A from aeroponically grown *Withania somnifera* **pp 2210–2214**
Ya-ming Xu, Marilyn T. Marron, Emily Seddon, Steven P. McLaughlin, Dennis T. Ray, Luke Whitesell, A. A. Leslie Gunatilaka *



Aeroponic culture of *Withania somnifera* afforded 2,3-dihydrowithaferin A-3β-*O*-sulfate (**1**), a new natural product and a potential prodrug of withaferin A (**2**).

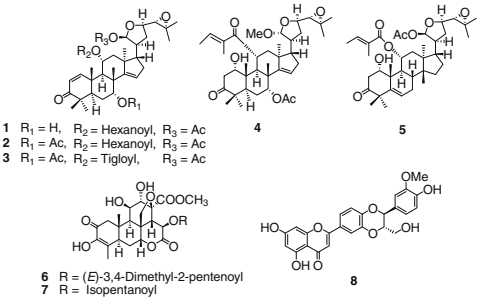
Antiproliferative cardenolide glycosides of *Elaeodendron alluaudianum* from the Madagascar Rainforest **pp 2215–2218**
Yanpeng Hou, Shugeng Cao, Peggy Brodie, Martin Callmander, Fidisoa Ratovoson, Richard Randrianaivo, Etienne Rakotobe, Vincent E. Rasamison, Stephan Rakotonandrasana, Karen TenDyke, Edward M. Suh, David G. I. Kingston *



1 R = CH_2OH
2 R = CHO

Bioactivity-guided isolation of cytotoxic constituents of *Brucea javanica* collected in Vietnam **pp 2219–2224**
Li Pan, Young-Won Chin, Hee-Byung Chai, Tran Ngoc Ninh, Djaja Djendoel Soejarto, A. Douglas Kinghorn *

Eight compounds were isolated from a chloroform-soluble subfraction of the methanol extract of the combined twigs, leaves, and inflorescence of *Brucea javanica* collected in Vietnam. Among these compounds, **1**–**5** were characterized as five new triterpenoids. Two known quassinoids, bruceantin (**6**) and bruceine A (**7**), demonstrated highly inhibitory activities against a small panel of human cancer cell lines, and the cytotoxic potencies of **6** and **7** for the MCF-7 cell line were increased in the presence of (−)-hydnocarpin (**8**).



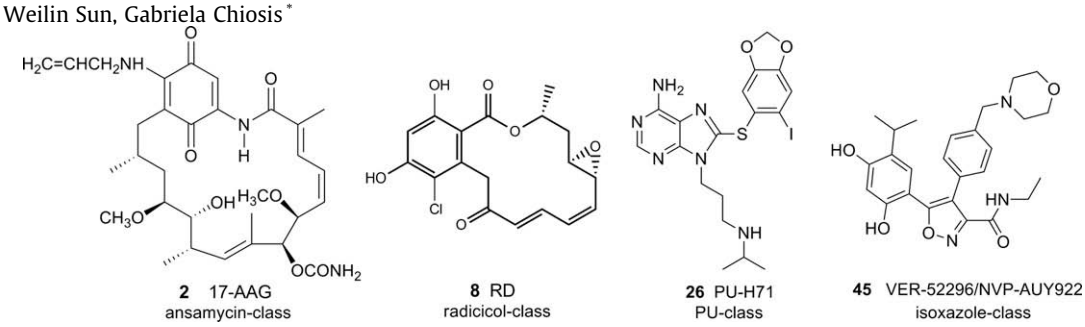
1 R_1 = H, R_2 = Hexanoyl, R_3 = Ac
2 R_1 = Ac, R_2 = Hexanoyl, R_3 = Ac
3 R_1 = Ac, R_2 = Tigloyl, R_3 = Ac

4 **5**

6 R = (*E*)-3,4-Dimethyl-2-pentenoyl
7 R = Isopentanoyl

8

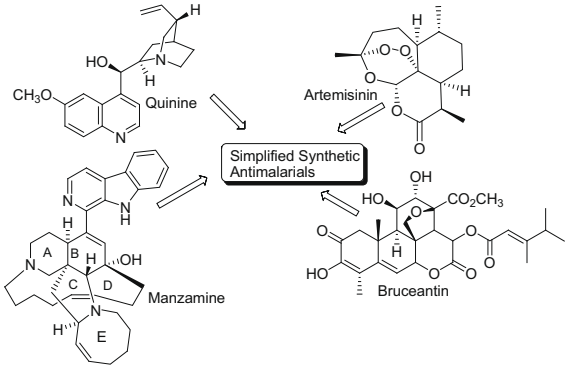
Discovery and development of heat shock protein 90 inhibitors pp 2225–2235
Tony Taldone, Weilin Sun, Gabriela Chiosis *



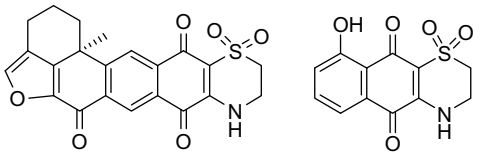
The different classes of Hsp90 inhibitors are reviewed including natural products such as geldanamycin and radicicol and synthetic inhibitors comprised of purines, pyrazoles, isoxazoles and other scaffolds.

Synthetic medicinal chemistry of selected antimalarial natural products pp 2236–2275
Vipan Kumar, Aman Mahajan, Kelly Chibale *

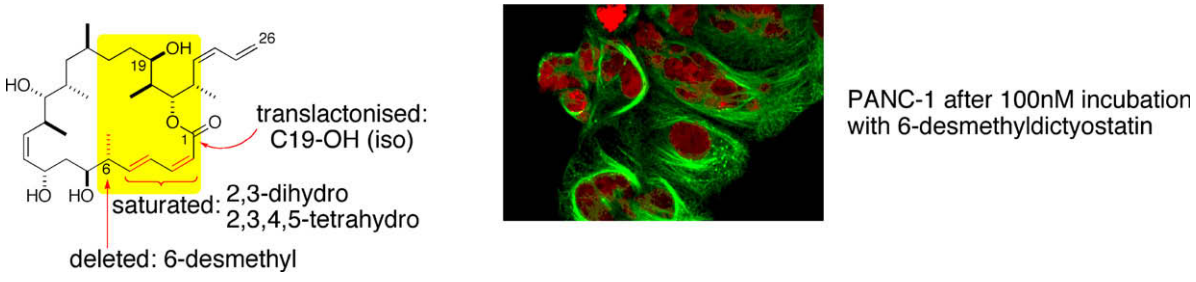
A variety of natural products have served as templates for the development of structurally simpler analogues that either served or continue to serve as effective antimalarials.



Bioactivities of simplified adociaquinone B and naphthoquinone derivatives against Cdc25B, MKP-1, and MKP-3 phosphatases pp 2276–2281
Shugeng Cao, Brian T. Murphy, Caleb Foster, John S. Lazo, David G. I. Kingston *

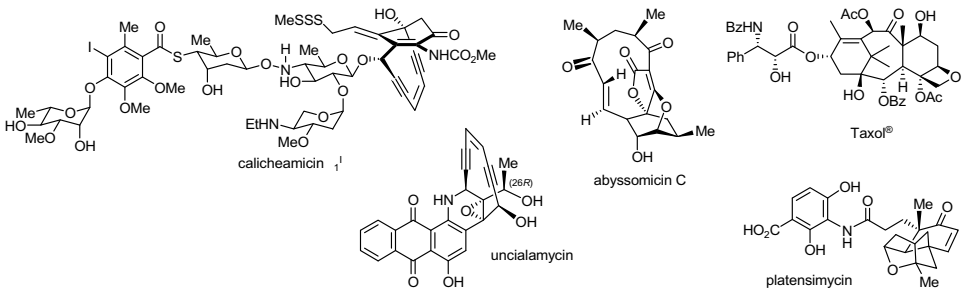


Total synthesis and biological evaluation of novel C2–C6 region analogues of dictyostatin pp 2282–2289
Ian Paterson*, Nicola M. Gardner, Esther Guzmán, Amy E. Wright



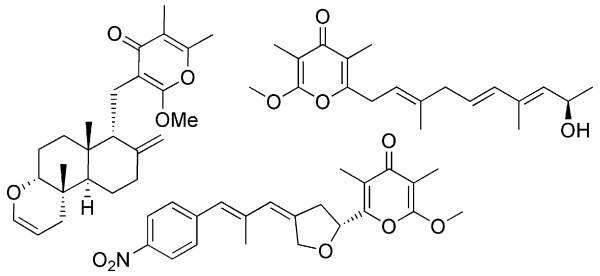
Novel analogues of the microtubule-stabilising agent dictyostatin were designed, synthesised and evaluated in vitro for growth inhibition against a range of human cancer cell lines.

From nature to the laboratory and into the clinic **pp 2290–2303**
K. C. Nicolaou*, Jason S. Chen, Stephen M. Dalby



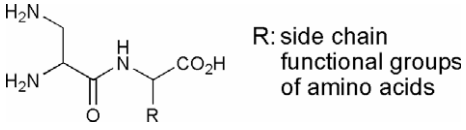
Influential synthetic studies in the authors' laboratory with a number of important naturally occurring substances, including calicheamicin γ_1^I, Taxol®, uncialamycin, abyssomicin C, and platensimycin, are briefly discussed.

γ-Pyrone natural products—A privileged compound class provided by nature **pp 2304–2309**
Wolfram Wilk, Herbert Waldmann*, Markus Kaiser*



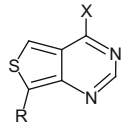
REGULAR ARTICLES

N-Terminal 2,3-diaminopropionic acid (Dap) peptides as efficient methylglyoxal scavengers to inhibit advanced glycation endproduct (AGE) formation **pp 2310–2320**
N. André Sasaki*, Maria Concepcion Garcia-Alvarez, Qian Wang, Ludmila Ermolenko, Gisèle Franck, Naïma Nhiri, Marie-Thérèse Martin, Nicolas Audic, Pierre Potier



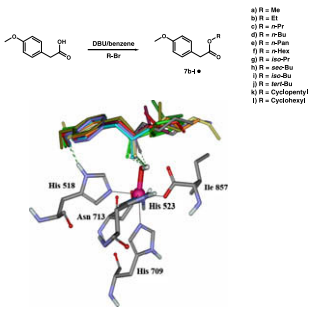
N-Terminal Dap-containing dipeptides were evaluated as a new type of efficient α-dicarbonyl scavengers for the inhibition of AGEs.

Synthesis and antiviral evaluation of thieno[3,4-*d*]pyrimidine *C*-nucleoside analogues of 2′,3′-dideoxy- and 2′,3′-dideoxy-2′,3′-didehydro-adenosine and -inosine **pp 2321–2326**
Marie Hamann, Claire Pierra*, Jean-Pierre Sommadossi, Chiara Musiu, Luana Vargiu, Michel Liuzzi, Richard Storer, Gilles Gosselin

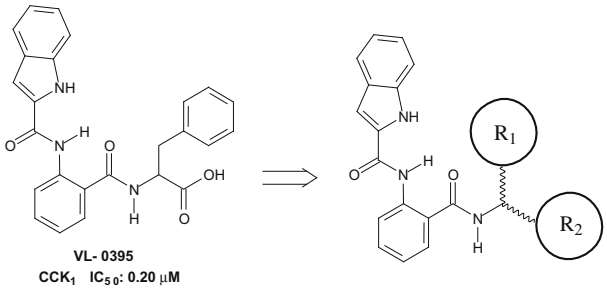


Several thieno[3,4-*d*]pyrimidine nucleoside analogs have been synthesized and evaluated against HIV. None of the tested compounds exhibited any significant antiviral effect, while two of them showed some cytotoxicity.

Design and synthesis of 4-methoxyphenylacetic acid esters as 15-lipoxygenase inhibitors and SAR comparative studies of them pp 2327–2335
Hamid Sadeghian*, Neda Attaran, Zeinab Jafari, Mohammad Reza Saberi, Mehdi Pordel, Mohammad Mahdi Riazi

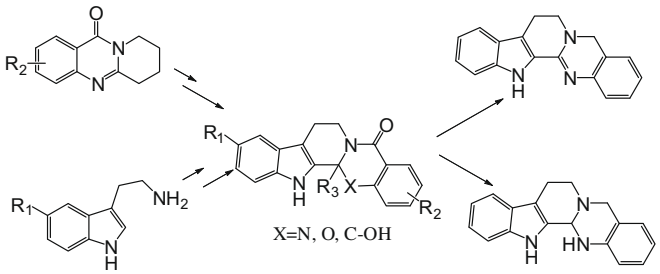


Anthranilic acid based CCK_1 receptor antagonists: Blocking the receptor with the same 'words' of the endogenous ligand pp 2336–2350
Lucia Lassiani, Michela V. Pavan, Federico Berti, George Kokotos, Theodoros Markidis, Laura Mennuni, Francesco Makovec, Antonio Varnavas*



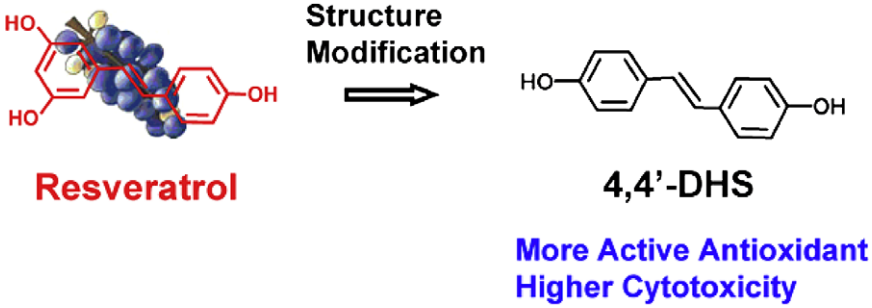
The anthranilic acid based lead compound VL-0395, which represent the more recent prototype of CCK_1 receptor antagonist, has been modified using, instead of Phe, aminoacids belonging to the primary structure of CCK-8 and other not coded residues.

Synthesis and vasodilator effects of rutaecarpine analogues which might be involved transient receptor potential vanilloid subfamily, member 1 (TRPV1) pp 2351–2359
Zhuo Chen, Gaoyun Hu*, Dai Li, Jun Chen, Yuanjian Li, Huayong Zhou, Ye Xie



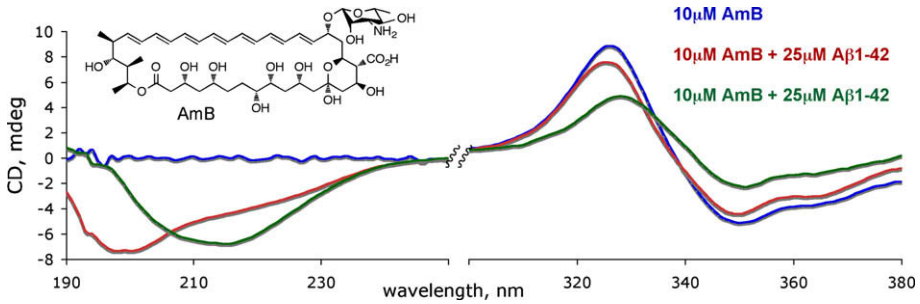
We designed and synthesized different kinds of rutaecarpine analogues. Their vasodilator effects were screened. Further studies showed the effects might be related with TRPV1.

4,4′-Dihydroxy-*trans*-stilbene, a resveratrol analogue, exhibited enhanced antioxidant activity and cytotoxicity pp 2360–2365
Gui-Juan Fan, Xiao-Da Liu, Yi-Ping Qian, Ya-Jing Shang, Xiu-Zhuang Li, Fang Dai*, Jian-Guo Fang, Xiao-Ling Jin, Bo Zhou*



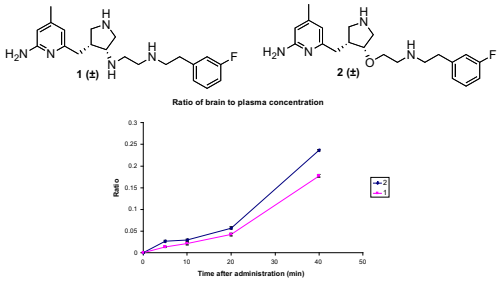
4,4′-Dihydroxy-*trans*-stilbene (4,4′-DHS) exhibits remarkably higher antioxidant activity and cytotoxicity against HL-60 cells than resveratrol.

Amphotericin B interactions with soluble oligomers of amyloid Aβ1-42 peptide **pp 2366–2370**
Nicholas W. Smith, Onofrio Annunziata, Sergei V. Dzyuba *



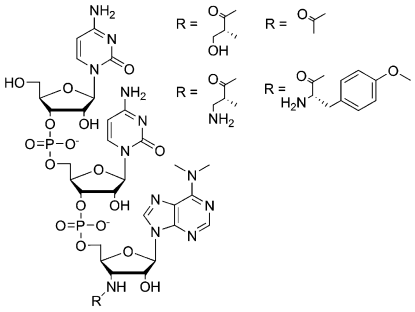
Amphotericin B is a potential spectroscopic probe for a random coil and β-sheet conformations of soluble Aβ1-42 oligomers.

Analogues of 2-aminopyridine-based selective inhibitors of neuronal nitric oxide synthase with increased bioavailability **pp 2371–2380**
Graham R. Lawton, Hantamalala Ralay Ranaivo, Laura K. Chico, Haitao Ji, Fengtian Xue, Pavel Martásek, Linda J. Roman, D. Martin Watterson, Richard B. Silverman *

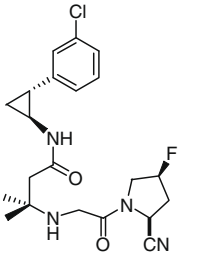


Synthesis of puromycin derivatives with backbone-elongated substrates and associated translation inhibitory activities **pp 2381–2387**
Keigo Mizusawa, Kenji Abe, Shinsuke Sando *, Yasuhiro Aoyama *

The synthesis of puromycin derivatives with backbone-elongated substrates is reported.

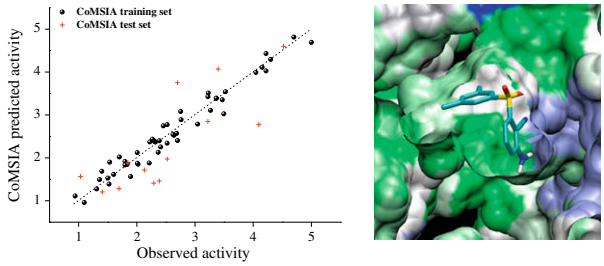


Novel *trans*-2-aryl-cyclopropylamine analogues as potent and selective dipeptidyl peptidase IV inhibitors **pp 2388–2399**
Ting-Yueh Tsai, Tsu Hsu, Chiung-Tong Chen, Jai-Hong Cheng, Teng-Kuang Yeh, Xin Chen, Chung-Yu Huang, Chung-Nien Chang, Kai-Chia Yeh, Su-Huei Hsieh, Chia-Hui Chien, Yi-Wei Chang, Chih-Hsiang Huang, Yu-Wen Huang, Chen-Lung Huang, Ssu-Hui Wu, Min-Hsien Wang, Cheng-Tai Lu, Yu-Sheng Chao, Weir-Torn Jiaang *



24b
DPP-IV IC_{50} = 15 nM

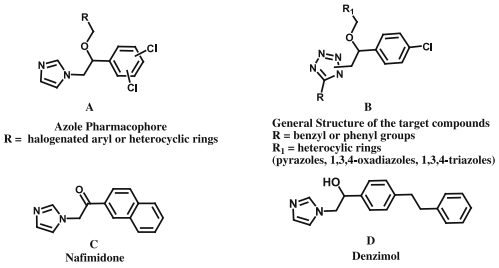
Receptor- and ligand-based 3D-QSAR study for a series of non-nucleoside HIV-1 reverse transcriptase inhibitors **pp 2400–2409**
Rongjing Hu, Florent Barbault, Michel Delamar*, Ruisheng Zhang*



A CoMSIA model with high predictive ability is developed. Favorable positions for bulky, hydrophobic and H-bond donor or acceptor substituents are discussed.

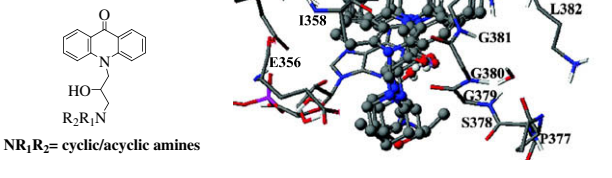
Azole antimicrobial pharmacophore-based tetrazoles: Synthesis and biological evaluation as potential antimicrobial and anticonvulsant agents **pp 2410–2422**
Sherif A. F. Rostom*, Hayam M. A. Ashour, Heba A. Abd El Razik, Abd El Fattah H. Abd El Fattah, Nagwa N. El-Din

This study presents the synthesis and antimicrobial evaluation of a new series of substituted tetrazoles that are structurally related to the famous antimicrobial azole pharmacophore. Antimicrobial evaluation revealed that twenty compounds were able to display variable growth inhibitory effects on the tested Gram positive and Gram negative bacteria with special efficacy against the Gram positive strains. Meanwhile, six compounds exhibited some moderate antifungal activity against *Candida albicans* and *Aspergillus fumigatus*. Compounds **16**, **18**, **24** and **27** proved to be the most active antibacterial members within this study, especially **18** against *Staphylococcus aureus* that was equipotent to ampicillin. On the other hand, twelve compounds were screened for their preliminary anticonvulsant activity against subcutaneous metrazole (ScMet) and maximal electroshock (MES) induced seizures in mice. The results revealed that five compounds namely; **3**, **5**, **13**, **21**, and **24** were able to display noticeable anticonvulsant activity in both tests at 100mg/kg dose level. Compounds **5** and **21** proved to the most active anticonvulsant members in this study with special high activity in the ScMet assay (% protection: 100% and 80%, respectively).



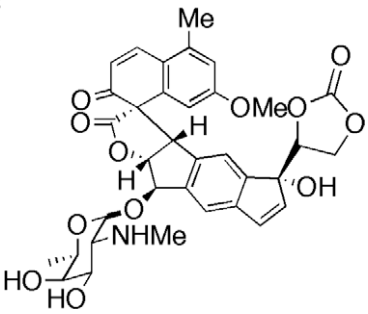
Search for MDR modulators: Design, syntheses and evaluations of N-substituted acridones for interactions with *p*-glycoprotein and Mg^{2+} **pp 2423–2427**
Palwinder Singh*, Jatinder kaur, Prabhjit Kaur, Satwinderjeet Kaur

Acridones with a hydroxylamine chain at nitrogen show appreciable interactions with *p*-gp and Mg^{2+}.

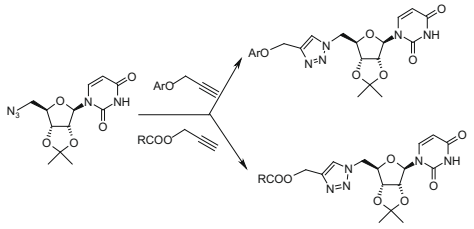


Designed DNA probes from the neocarzinostatin family: Impact of glycosyl linkage stereochemistry on bulge base binding **pp 2428–2432**
Dong Ma, Yiqing Lin, Ziwei Xiao, Lizzy Kappen, Irving H. Goldberg, Amy E. Kallmerten, Graham B. Jones*

The metabolite NCSi-gb of the natural product neocarzinostatin (NCS) shows strong binding affinity for two base bulges in DNA. Given the significance of DNA bulges in a variety of disease related processes, we undertook an examination of the structural requirements for bulge-drug binding. Using readily accessible mimics of NCSi-gb, we show that the stereochemistry of the aminolucosyl group plays a pivotal role, contributing to observed affinity and specificity of bulge binding.

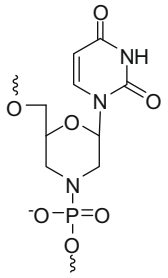


Exploration of click reaction for the synthesis of modified nucleosides as chitin synthase inhibitors **pp 2433–2440**
Preeti M. Chaudhary, Sayalee R. Chavan, Fazal Shirazi, Meenakshi Razdan, Prachi Nimkar, Shailaja P. Maybhate, Anjali P. Likhite, Rajesh Gonnade, Braja G. Hazara, Mukund V. Deshpande, Sunita R. Deshpande *



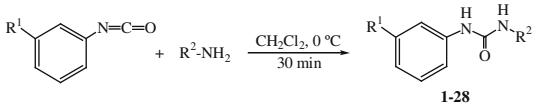
A click reaction approach toward the synthesis of new 1,2,3-triazolyl uridine derivatives as chitin synthase inhibitors was adopted by Cu(I)-catalyzed 1,3-dipolar cycloaddition of 5′-azido-5′-deoxy-2′,3′-*O*-(1-methylethylidene)uridine with propargylated ether of phenols and propargyl ester of acids.

RNA interference in mammalian cells by siRNAs modified with morpholino nucleoside analogues **pp 2441–2446**
Nan Zhang, Chunyan Tan, Puqin Cai, Peizhuo Zhang, Yufen Zhao, Yuyang Jiang *



The synthesis, gene silencing activity, and biostability of siRNAs modified with morpholino nucleoside analogues is reported.

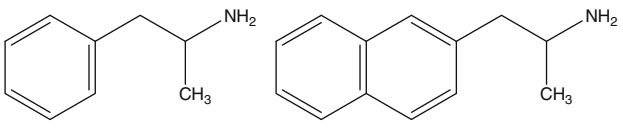
Unsymmetrically disubstituted urea derivatives: A potent class of antiglycating agents **pp 2447–2451**
Khalid M. Khan*, Sumayya Saeed, Muhammad Ali, Madiha Gohar, Javariya Zahid, Ambreen Khan, Shahnaz Perveen, M. Iqbal Choudhary



1-28

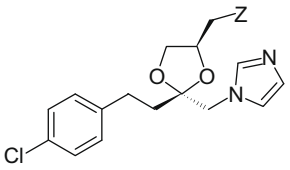
A series of unsymmetrically disubstituted urea derivatives **1–28** has been synthesized and screened for their antiglycation activity in vitro. Where R^1 and R^2 may be any alkyl or aryl group.

Naphthylisopropylamine and *N*-benzylamphetamine derivatives as monoamine oxidase inhibitors **pp 2452–2460**
Marcelo Vilches-Herrera, Juan Miranda-Sepúlveda, Marco Rebolledo-Fuentes, Angélica Fierro, Susan Lühr, Patricio Iturriaga-Vasquez, Bruce K. Cassels, Miguel Reyes-Parada *



*K*i MAO-A = 12.20 μM *K*i MAO-A = 0.42 μM

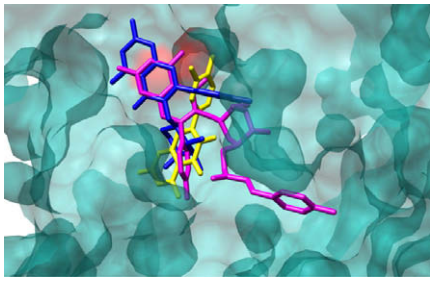
Synthesis and evaluation of imidazole–dioxolane compounds as selective heme oxygenase inhibitors: Effect of substituents at the 4-position of the dioxolane ring **pp 2461–2475**
Jason Z. Vlahakis, Maaike Hum, Mona N. Rahman, Zongchao Jia, Kanji Nakatsu, Walter A. Szarek *



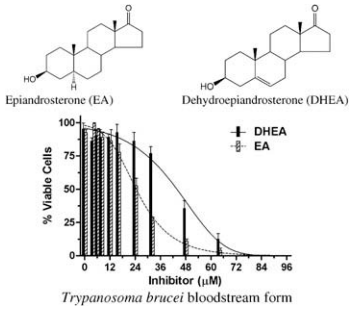
A series of imidazole–dioxolane compounds were synthesized and evaluated as selective heme oxygenase inhibitors.

Discovery of novel *Trypanosoma cruzi* glyceraldehyde-3-phosphate dehydrogenase inhibitors **pp 2476–2482**
Renato F. Freitas, Igor M. Prokopczyk, Aderson Zottis, Glaucius Oliva, Adriano D. Andricopulo, Maria Teresa S. Trevisan, Wagner Vilegas, Maria Goretti V. Silva *, Carlos A. Montanari *

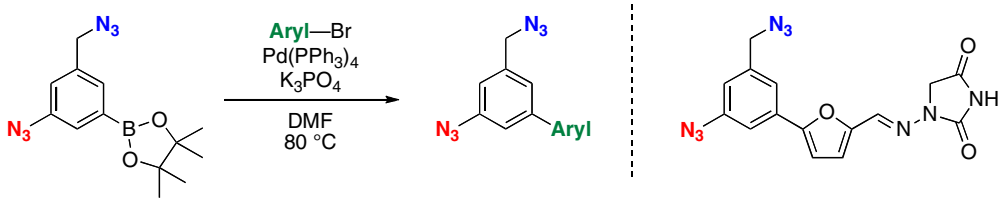
Virtual screening strategies can be very attractive in the discovery and development of new drugs for neglected diseases. As part of our ongoing efforts to find novel potential inhibitors of *Trypanosoma cruzi* GAPDH aimed at treating Chagaśdisease, we have used a combination of ligand-based and structure-based techniques to screen an in-house natural product database in a sequential manner. In an information overloaded chemical space, the use of techniques from complementary approaches resulted in the identification of seven bioactive natural products that include anacardic acids, flavonoid derivatives and one glucosylxanthone.



Inhibition of *Trypanosoma brucei* glucose-6-phosphate dehydrogenase by human steroids and their effects on the viability of cultured parasites **pp 2483–2489**
Artur T. Cordeiro*, Otavio H. Thiemann, Paul A. M. Michels

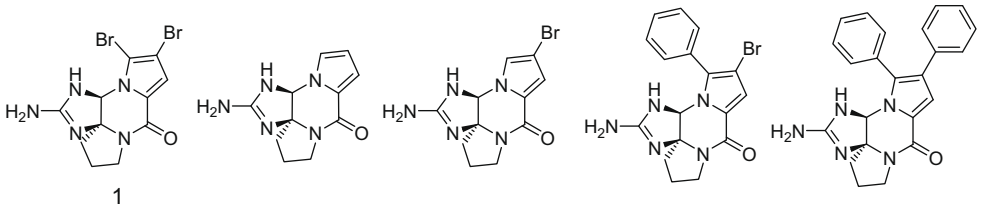


Facile synthesis of diazido-functionalized biaryl compounds as radioisotope-free photoaffinity probes by Suzuki–Miyaura coupling **pp 2490–2496**
Takamitsu Hosoya*, Atsushi Inoue, Toshiyuki Hiramatsu, Hiroshi Aoyama, Takaaki Ikemoto, Masaaki Suzuki



Suzuki–Miyaura coupling of 3-azido-5-(azidomethyl)phenylboronic acid pinacol ester with various aryl bromides affords corresponding diazido-functionalized biaryl compounds in good yields providing an easy access to RI-free photoaffinity probes possessing biaryl structure. By using this method, a novel diazido-functionalized dantrolene analog with selective inhibitory effect on physiological Ca^{2+} release from sarcoplasmic reticulum in mouse skeletal muscle was prepared.

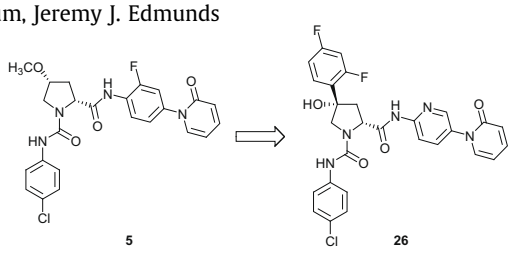
(−)-Dibromophakellin: An α_{2B} adrenoceptor agonist isolated from the Australian marine sponge, *Acanthella costata* **pp 2497–2500**
Rohan A. Davis, Gregory A. Fechner, Melissa Sykes, Agatha Garavelas, David M. Pass, Anthony R. Carroll, Rama Addepalli, Vicky M. Avery, John N. A. Hooper, Ronald J. Quinn *



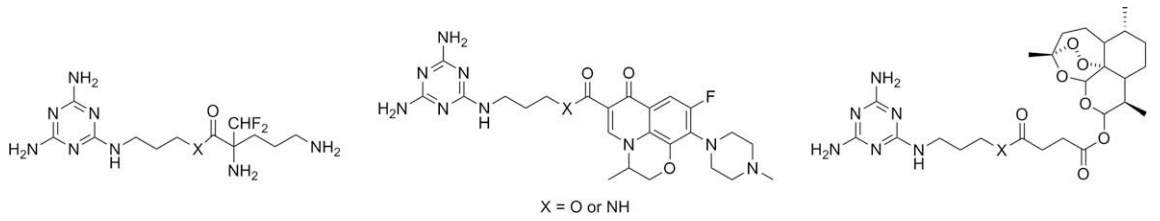
Bioassay-guided fractionation of the organic extract from the marine sponge *Acanthella costata* identified (−)-dibromophakellin (**1**) as an α_{2B} adrenoceptor agonist, with an EC_{50} of 4. 2 μM. A series of small-scale synthetic reactions were performed on this marine natural product in order to provide SAR data about the pyrrole ring.

Exploration of 4,4-disubstituted pyrrolidine-1,2-dicarboxamides as potent, orally active Factor Xa inhibitors with extended duration of action **pp 2501–2511**
Chad A. Van Huis, Agustin Casimiro-Garcia*, Christopher F. Bigge, Wayne L. Cody, Danette A. Dudley, Kevin J. Filipski, Ronald J. Heemstra, Jeffrey T. Kohrt, Robert J. Leadley Jr., Lakshmi S. Narasimhan, Thomas McClanahan, Igor Mochalkin, Michael Pamment, J. Thomas Peterson, Vaishali Sahasrabudhe, Robert P. Schaum, Jeremy J. Edmunds

With the intent to improve upon the projected human half-life of the previously disclosed Factor Xa inhibitor **5**, a series of 4,4-disubstituted pyrrolidine-1,2-dicarboxamides were explored. This work led to the discovery of **26**, a selective, orally bioavailable, and efficacious Factor Xa inhibitor.

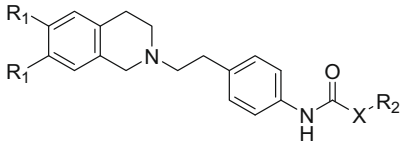


Targeted delivery of compounds to *Trypanosoma brucei* using the melamine motif **pp 2512–2523**
Constance Chollet, Alessandro Baliani, Pui Ee Wong, Michael P. Barrett, Ian H. Gilbert *

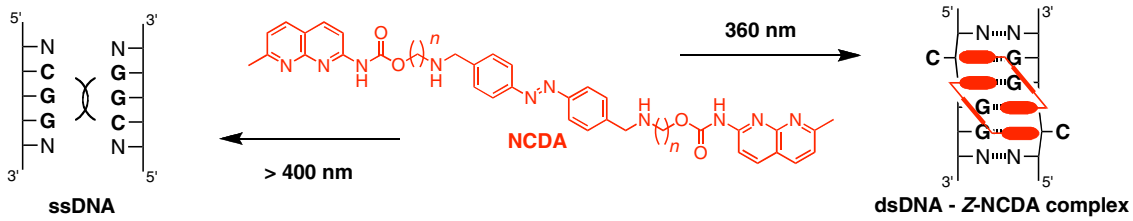


Melamine conjugates of DFMO, fluoroquinolones and artesunate designed for selective uptake by *Trypanosoma brucei*.

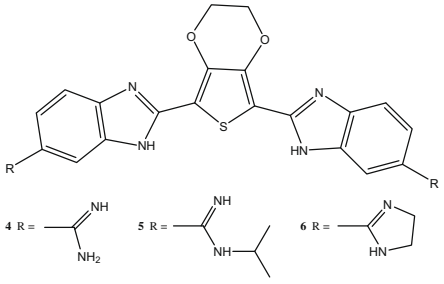
Synthesis and biological evaluation of a small molecule library of 3rd generation multidrug resistance modulators **pp 2524–2535**
Werner Klinkhammer, Henrik Müller, Christoph Globisch, Ilza K. Pajeva, Michael Wiese *



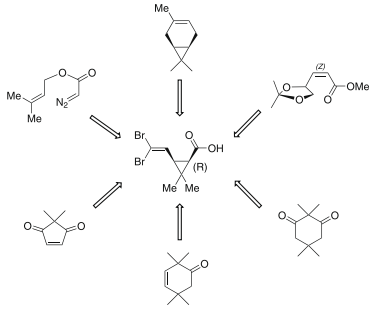
The effect of linker length on binding affinity of a photoswitchable molecular glue for DNA **pp 2536–2543**
Chikara Dohno, Shin-nosuke Uno, Shun Sakai, Mika Oku, Kazuhiko Nakatani *



Effect of 3,4-ethylenedioxy-extension of thiophene core on the DNA/RNA binding properties and biological activity of bisbenzimidazole amidines **pp 2544–2554**
Ivana Stolić, Katarina Mišković, Anahi Magdaleno, Ariel Mariano Silber, Ivo Piantanida, Miroslav Bajić *, Ljubica Glavaš-Obrovac *

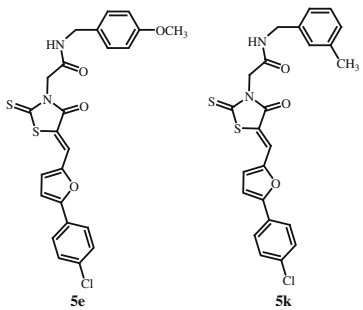


Inspired by flowers: Synthetic routes to scalemic deltamethrinic acid **pp 2555–2575**
Alain Krief *, Stephane Jeanmart, Adrian Kremer

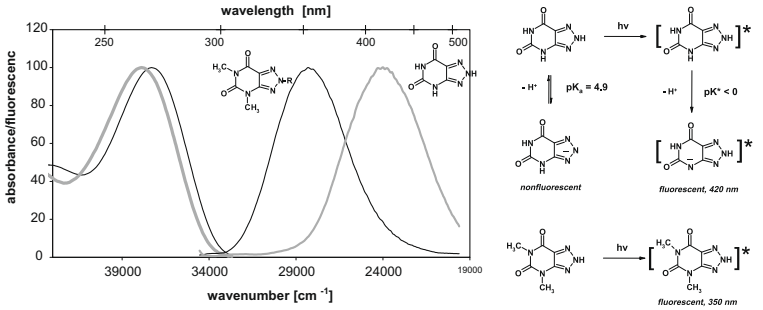


Synthesis of 2-(5-((5-(4-chlorophenyl)furan-2-yl)methylene)-4-oxo-2-thioxothiazolidin-3-yl)acetic acid derivatives and evaluation of their cytotoxicity and induction of apoptosis in human leukemia cells **pp 2576–2584**
S. Chandrappa, C. V. Kavitha, M. S. Shahabuddin, K. Vinaya, C. S. Ananda Kumar, S. R. Ranganatha, Sathees C. Raghavan *, K. S. Rangappa *

Novel 2-(5-((5-(4-chlorophenyl)furan-2-yl)methylene)-4-oxo-2-thioxothiazolidin-3-yl)acetic acid derivatives **5(a–l)** were synthesized in good yield. To rationalize the role of electron donating group in the induction of cytotoxicity we have chosen two molecules (**5e** and **5k**) having different electron donating group at different positions. LDH assay, Flow cytometric analysis and DNA fragmentation suggest that **5e** is more cytotoxic and able to induce the apoptosis.

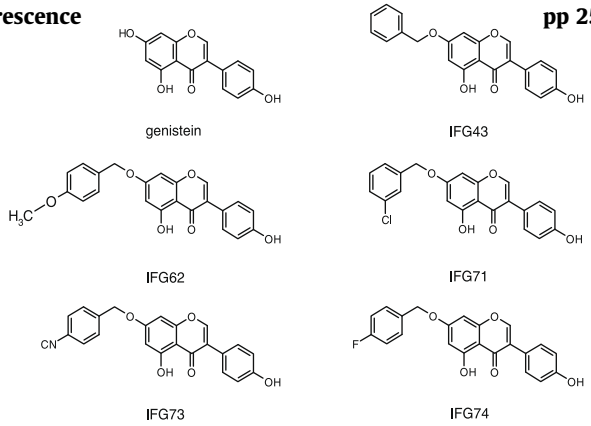


Fluorescence emission properties of 8-aza analogues of caffeine, theophylline, and related *N*-alkyl xanthines **pp 2585–2591**
Grzegorz Mędza, Jacek Wierzchowski*, Borys Kierdaszuk, David Shugar

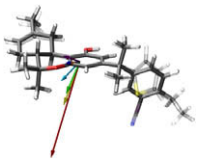


Interaction of genistein benzyl derivatives with lipid bilayers—fluorescence spectroscopic and calorimetric study **pp 2592–2597**
J. Maniewska, G. Grynkiewicz, W. Szeja, A. B. Hendrich *

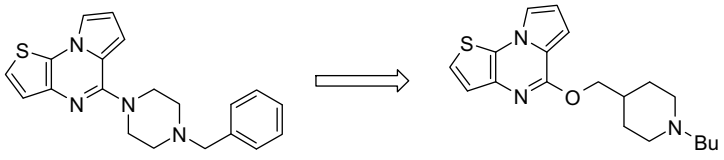
Newly synthesized genistein benzyl derivatives perturb polar and hydrophobic region of lipid bilayer. Their interaction with membrane depends on its physical state.



Quantitative structure–activity relationship (QSAR) for a series of novel cannabinoid derivatives using descriptors derived from semi-empirical quantum-chemical calculations **pp 2598–2606**
Antonio M. Ferreira*, Mathangi Krishnamurthy, Bob M. Moore II, David Finkelstein, Donald Bashford

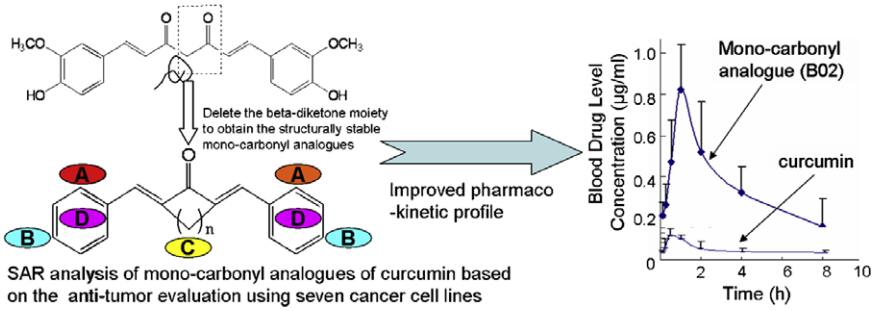


Novel antagonists of serotonin-4 receptors: Synthesis and biological evaluation of pyrrolothienopyrazines **pp 2607–2622**
Stéphane Lemaître, Alban Lepailleur, Ronan Bureau, Sabrina Butt-Gueulle, Véronique Lelong-Boulouard, Pascal Duchatelle, Michel Boulouard, Aline Dumuis, Cyril Daveu, Frank Lezoualc'h, Bruno Pfeiffer, François Dauphin, Sylvain Rault *



From 5-HT$_3$ to 5-HT$_4$ and 5-HT$_3$/5-HT$_4$ ligands

Exploration and synthesis of curcumin analogues with improved structural stability both in vitro and in vivo as cytotoxic agents **pp 2623–2631**
Guang Liang, Lili Shao, Yi Wang, Chengguang Zhao, Yanhui Chu, Jian Xiao, Yu Zhao, Xiaokun Li*, Shulin Yang*



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*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

This issue is a commissioned Symposium-in-Print containing 21 articles (research papers and reviews) on the basic theme of Natural Products as biological probes and leads to drugs. The articles in the symposium are organized to show the utility of Nature's privileged structures and thus cover areas ranging from biosynthesis, the starting point of all natural compounds, through current discoveries from microbes, marine invertebrates and plants. The symposium then continues with articles showing the influence that such discoveries, when coupled to modern techniques of structure determination including absolute syntheses, may have on the derivation of biological probes and drug candidates based on Nature's Pharmacopoeia.

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

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