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Bioorganic &
Medicinal
Chemistry

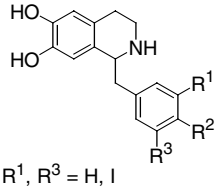
Bioorganic & Medicinal Chemistry Vol. 14, No. 6, 2006

Contents

ARTICLES

1-Benzyl-1,2,3,4-tetrahydroisoquinoline-6,7-diols as novel affinity and photoaffinity probes for β-adrenoceptor subtypes **pp 1684–1697**

Victor I. Nikulin, Igor M. Rakov, Joseph E. De Los Angeles, Ratna C. Mehta, LeNe'Sheya Y. Boyd, Dennis R. Feller and Duane D. Miller*

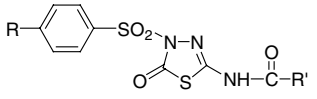


R^1, R^3 = H, I

R^2 = $NHCOCH_2Cl$, $NHCOCH_2Br$ NCS, N_3, COPh

New 1,3,4-thiadiazole derivatives endowed with analgesic and anti-inflammatory activities **pp 1698–1705**

Silvia Schenone,* Chiara Brullo, Olga Bruno, Francesco Bondavalli, Angelo Ranise, Walter Filippelli, Barbara Rinaldi, Annalisa Capuano and Giuseppe Falcone



3 a-t

New 2,4-disubstituted 1,3,4-thiadiazole derivatives **3a**–**t** were synthesized and tested for pharmacological actions. Compounds showed interesting analgesic and anti-inflammatory activity in vivo; ulcerogenic action was also reported.

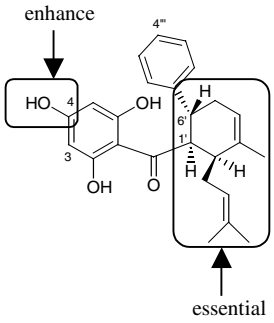
The antioxidant activity of glucosamine hydrochloride in vitro **pp 1706–1709**

Ronge Xing, Song Liu, Zhanyong Guo, Huahua Yu, Cuiping Li, Xia Ji, Jinhua Feng and Pengcheng Li*

The antioxidant activity of glucosamine hydrochloride in vitro was researched.

Anti-HIV-1 protease activity of compounds from *Boesenbergia pandurata* **pp 1710–1714**
Sarot Cheenpracha, Chatchanok Karalai, Chanita Ponglimanont, Sanan Subhadhirasakul and Supinya Tewtrakul*

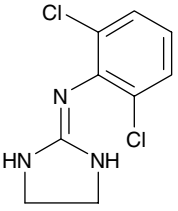
Searching for anti-HIV-1 protease (PR) inhibitors of Thai medicinal plants led to the isolation of a new cyclohexenyl chalcone named panduratin C (**1**) and chalcone derivatives (**2**–**6**) from the methanol extract of *Boesenbergia pandurata* rhizomes. The known compounds were identified to be panduratin A (**2**), hydroxypanduratin A (**3**), helichrysetin (**4**), 2′,4′,6′-trihydroxyhydrochalcone (**5**), and uvangoletin (**6**). It was found that **3** possessed the most potent anti-HIV-1 PR activity with an IC_{50} value of 5.6 μM, followed by **2** (IC_{50} = 18.7 μM), whereas others exhibited mild activity. Structure–activity relationships of these compounds on anti-HIV-1 PR activity are summarized as follows: (1) hydroxyl moiety at position 4 conferred higher activity than methoxyl group; (2) prenylation of dihydrochalcone was essential for activity; (3) hydroxylation at position 4′ reduced activity; and (4) introduction of double bond at C1′ and C6′ of chalcone gave higher activity.



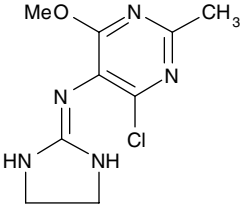
Hydroxypanduratin A

Theoretical study of structure, pK_a, lipophilicity, solubility, absorption, and polar surface area of some centrally acting antihypertensives **pp 1715–1728**
Milan Remko,* Marcel Swart and F. Matthias Bickelhaupt

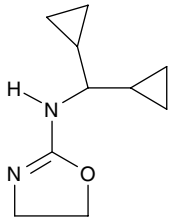
Structure, pK_a, lipophilicity, solubility, absorption, and polar surface area of 13 biologically active compounds, a class of potent agonists and antagonists of imidazoline receptors (including clinically useful clonidine, moxonidine, and rilmenidine), have been theoretically determined.



Clonidine



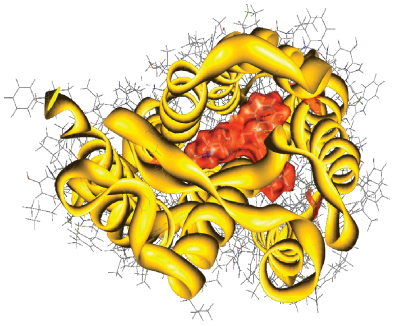
Moxonidine



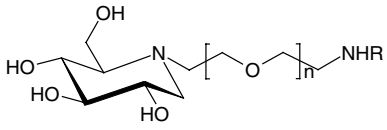
Rilmenidine

Enantiomeric *N*-methyl-4-piperidyl benzilates as muscarinic receptor ligands: Radioligand binding studies and docking studies to models of the three muscarinic receptors M1, M2 and M3 **pp 1729–1736**
Jana Selent, Wolfgang Brandt,* Dirk Pamperin and Berthold Göber

N-Methyl-4-piperidyl benzilates possess high affinity to muscarinic receptors. The binding site on muscarinic receptors (M1–M3) and the effect of structural variations of chiral *N*-methyl-4-piperidyl benzilates are investigated by molecular modelling and radioligand binding studies. Model of the M1 receptor with the potential binding site (red) for *N*-methyl-4-piperidyl benzilates depicted from the extracellular site.

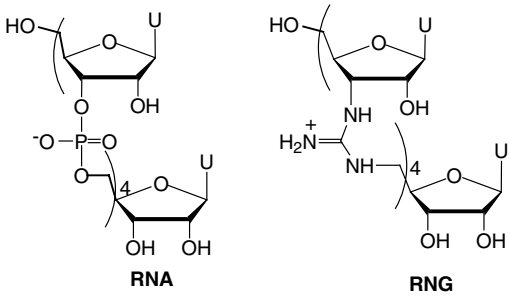


Fluorescently tagged iminoalditol glycosidase inhibitors as novel biological probes and diagnostics **pp 1737–1742**
Inge Lundt, Andreas J. Steiner, Arnold E. Stütz,* Chris A. Tarling, Stefan Ully, Stephen G. Withers and Tanja M. Wrodnigg

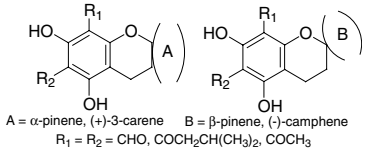


Ribonucleic guanidine demonstrates an unexpected marked preference for complementary DNA rather than RNA **pp 1743–1749**
Myunji Park, Joseph W. Toporowski and Thomas C. Bruice*

Replacement of the phosphodiester linkages of uridyl RNA with guanidinium linkers provides polycationic uridyl ribonucleic guanidine (RNG) as a putative antisense/antigene agent. Binding characteristics of uridyl-RNG and molecular dynamics results are discussed.

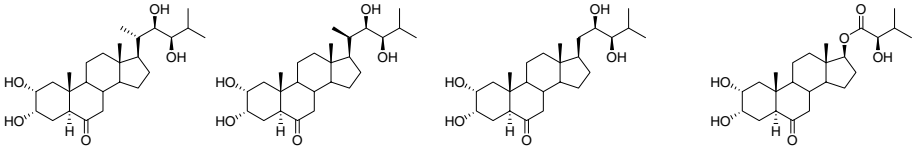


Biomimetic synthesis, antimicrobial, antileishmanial and antimalarial activities of euglobals and their analogues **pp 1750–1760**
Sandip B. Bharate, Kamlesh K. Bhutani, Shabana I. Khan, Babu L. Tekwani, Melissa R. Jacob, Ikhlas A. Khan and Inder Pal Singh*



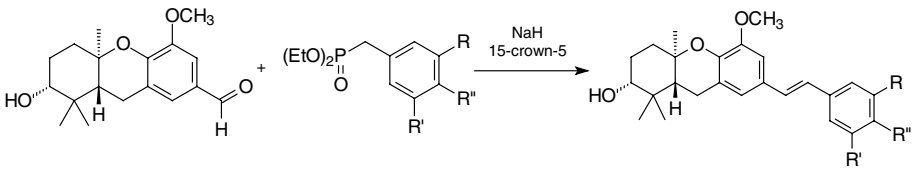
Naturally occurring phloroglucinol–terpene adducts, euglobals G1–G4 and 16 new analogues differing in nature of monoterpene moiety and acyl functionality were synthesized and evaluated for antimicrobial, antileishmanial and antimalarial activities. Some of these exhibited good antifungal and antileishmanial activities.

Synthesis of 26,27-bisnorcastasterone analogs and analysis of conformation–activity relationship for brassinolide-like activity **pp 1761–1770**
Shuji Yamamoto, Bunta Watanabe, Junko Otsuki, Yoshiaki Nakagawa,* Miki Akamatsu and Hisahi Miyagawa

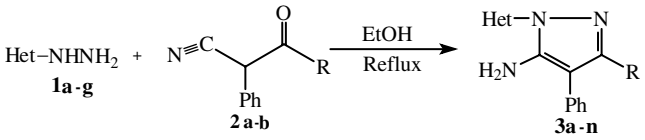


Three castasterone derivatives with varied side-chain moieties were synthesized stereoselectively from either stigmasterol or dehydroisoandrosterone, and their brassinolide-like activity was measured using a rice lamina-inclination assay.

Synthesis and structure–activity studies of schweinfurthin B analogs: Evidence for the importance of a D-ring hydrogen bond donor in expression of differential cytotoxicity **pp 1771–1784**
Jeffrey D. Neighbors, Maya S. Salnikova, John A. Beutler and David F. Wiemer*

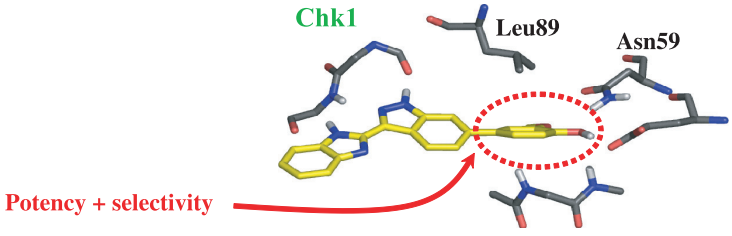


Synthesis and antibacterial activity of some new 1-heteroaryl-5-amino-3*H*/methyl-4-phenylpyrazoles **pp 1785–1791**
Ranjana Aggarwal,* Vinod Kumar, Parikshit Tyagi and Shiv P. Singh

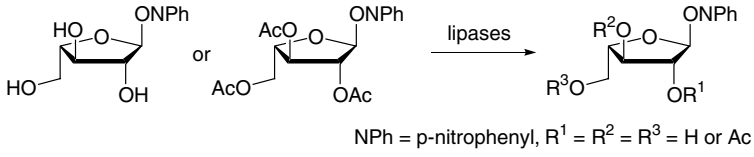


The regioselective synthesis of 1-heteroaryl-3*H*/methyl-5-amino-4-phenylpyrazoles **3a**–**n** was achieved by the treatment of heteroarylhydrazines **1a**–**g** with α-phenylacylacetonitrile **2a**–**b**, respectively. The structures of the compounds **3** were established by the combined use of ^{1}H and ^{13}C NMR spectroscopy. All the 14 compounds were tested for their in vitro antibacterial activity against three Gram-positive and two Gram-negative bacteria. Six compounds **3a**, **3d**, **3e**, **3g**, **3l**, and **3n** from this series were found to be equipotent or more potent than the commercial antibiotics (Linezolid and Cefroxime axetil).

Identification of a buried pocket for potent and selective inhibition of Chk1: Prediction and verification **pp 1792–1804**
Nicolas Foloppe,* Lisa M. Fisher, Geraint Francis, Rob Howes, Peter Kierstan and Andrew Potter

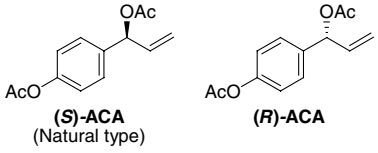


The acetates of *p*-nitrophenyl α-L-arabinofuranoside—regioselective preparation by action of lipases **pp 1805–1810**
Mária Mastihubová,* Jana Szemesová and Peter Biely



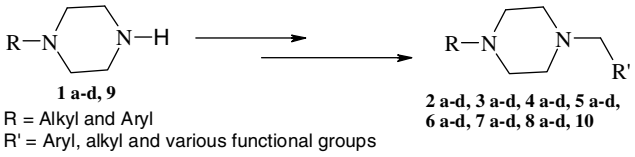
All possible di-*O*-acetates and mono-*O*-acetates of *p*-nitrophenyl α-L-arabinofuranoside were regioselectively prepared through acetylation or hydrolysis catalysed by lipases of various origin.

Lipase-catalyzed preparation of optically active 1′-acetoxychavicol acetates and their structure–activity relationships in apoptotic activity against human leukemia HL-60 cells **pp 1811–1818**
Hideki Azuma,* Keita Miyasaka, Tsuyoshi Yokotani, Taro Tachibana, Akiko Kojima-Yuasa, Isao Matsui-Yuasa and Kenji Ogino*



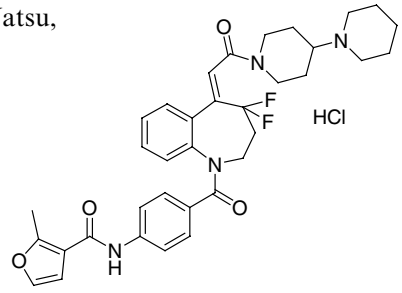
(1′*S*)-Acetoxychavicol acetate ((*S*)-**ACA**) and its enantiomer were prepared by a lipase-catalyzed esterification. Structure–activity relationships of **ACA** for apoptotic activity were investigated using these enantiomers and various racemic analogues.

Synthesis and antimicrobial activity of *N*-alkyl and *N*-aryl piperazine derivatives **pp 1819–1826**
Preeti Chaudhary, Rupesh Kumar, Akhilesh K. Verma,* Devender Singh, Vibha Yadav, Anil K. Chhillar, G. L. Sharma and Ramesh Chandra*

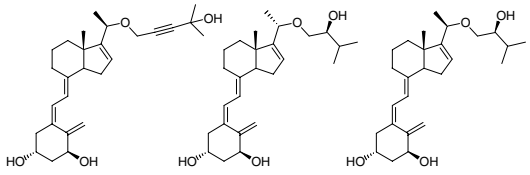


N-Alkyl and *N*-aryl derivatives of piperazines have been synthesized and screened for antibacterial and antifungal activities. All the synthesized compounds show potent antibacterial activity and were found to be less active against fungi. Compounds **4d** and **6a** were found to be very less toxic to human erythrocytes when compared with gentamicin.

Synthesis and biological activity of novel 4,4-difluorobenzazepine derivatives as non-peptide antagonists of the arginine vasopressin V_{1A} receptor **pp 1827–1837**
Yoshiaki Shimada,* Nobuaki Taniguchi, Akira Matsuhisa, Hiroaki Akane, Noriyuki Kawano, Takeshi Suzuki, Takahiko Tobe, Akio Kakefuda, Takeyuki Yatsu, Atsuo Tahara, Yuichi Tomura, Toshiyuki Kusayama, Koh-ichi Wada, Junko Tsukada, Masaya Orita, Takashi Tsunoda and Akihiro Tanaka



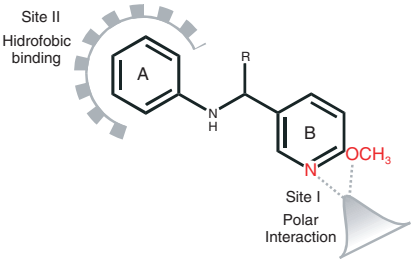
Novel vitamin D_3 antipsoriatic antedrugs: 16-En-22-oxa-1α,25-$(OH)_2D_3$ analogs **pp 1838–1850**
Kazuki Shimizu,* Akira Kawase, Tsuyoshi Haneishi, Yasuharu Kato, Takamitsu Kobayashi, Nobuo Sekiguchi, Tessai Yamamoto, Masaki Ishigai, Kazuo Tokuda, Tomochika Matsushita, Shin Shimaoka and Kazumi Morikawa



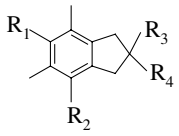
A series of 16-en-22-oxa-derivatives of vitamin D_3 based on the structure of maxacalcitol (**2**) were prepared.

Structure–activity relationship study of homoallylamines and related derivatives acting as antifungal agents **pp 1851–1862**
Fernando D. Suvire, Maximiliano Sortino, Vladimir V. Kouznetsov, Leonor Y. Vargas M, Susana A. Zacchino, Uriel Mora Cruz and Ricardo D. Enriz*

The synthesis, in vitro evaluation, and SAR studies of homoallylamines and related derivatives acting as antifungal agents are reported. Molecular modeling studies allow us to determine the pharmacophoric patron.



Design, synthesis, and biological evaluation of alcyopterosin A and illudalane derivatives as anticancer agents **pp 1863–1870**
Liliana M. Finkielsztein, Ana M. Bruno, Sergio G. Renou and Graciela Y. Moltrasio Iglesias*

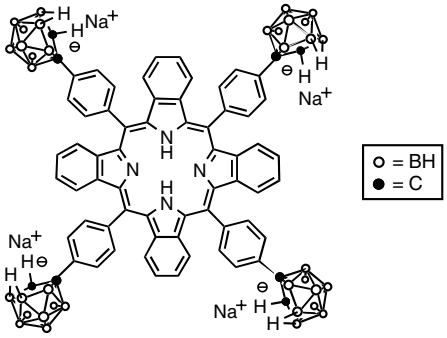


Alcyopterosin A
R_1: CH_2CH_2Cl
R_2: H
R_3, R_4: CH_3

Alcyopterosin A and novel illudalane derivatives were synthesized and evaluated for their anticancer activity.

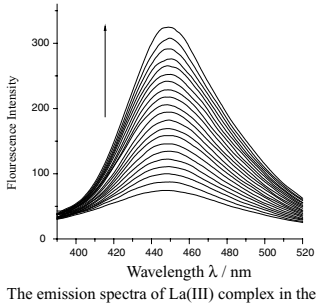
Synthesis, cellular uptake and animal toxicity of a tetra(carboranylphenyl)-tetrabenzoporphyrin **pp 1871–1879**
Vijay Gottumukkala, Owendi Ongayi, David G. Baker, Larry G. Lomax and M. Graça H. Vicente*

The total synthesis, cellular uptake, intracellular localization and animal toxicity of a tetra(*nido*-carboranylphenyl)-tetrabenzoporphyrinporphyrin are described and compared with a known tetra(*nido*-carboranyl)porphyrin.



Synthesis, characterization, cytotoxic activities, and DNA-binding properties of the La(III) complex with Naringenin Schiff-base **pp 1880–1888**
Bao-dui Wang, Zheng-Yin Yang,* Qin Wang, Ti-kuan Cai and Patrick Crewdson

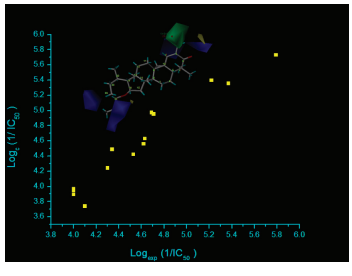
A new Naringenin Schiff-base ligand and its La(III) complex have been synthesized and characterized. Spectrometric titration and viscosity measurements indicate that two compounds strongly bind with calf-thymus DNA, presumably via an intercalation mechanism.



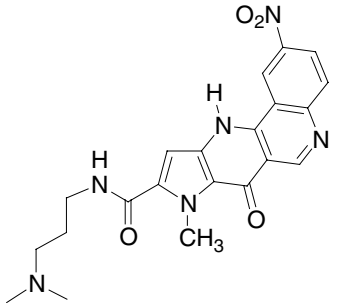
The emission spectra of La(III) complex in the presence of CT-DNA

Synthesis and comparative molecular field analysis (CoMFA) of argentatin B derivatives as growth inhibitors of human cancer cell lines **pp 1889–1901**
Hortensia Parra-Delgado, César M. Compadre, Teresa Ramírez-Apan, María J. Muñoz-Fambuena, R. Lilia Compadre, Patricia Ostrosky-Wegman and Mariano Martínez-Vázquez*

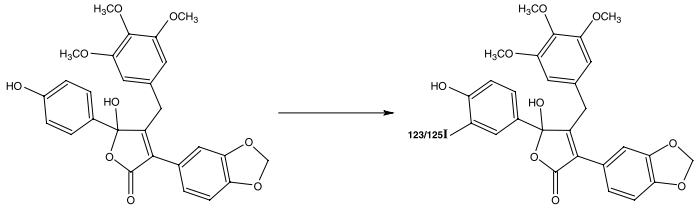
Synthesis, anticancer activity, and QSAR of 14 argentatin B analogs are described. Derivative 2-formyl-(16β,24*R*)-16,24-epoxy-25-hydroxycycloart-1-en-3-one was 35–50 times more potent than argentatin B to inhibit the growth of four human cancer cell lines. 3D-QSAR of K562 cell line growth inhibition was performed using the X-ray crystallographic structures of six derivatives as prototypes. Comparative molecular field analysis showed that a bulky group at C-2, a C1–C2 double bond, and a low electronic density near to C-25 increase the potency of these triterpenes. Experimental Log *P*s for argentatin B and one derivative were 1–2 Log units more hydrophilic than the C Log *P* predicted values.



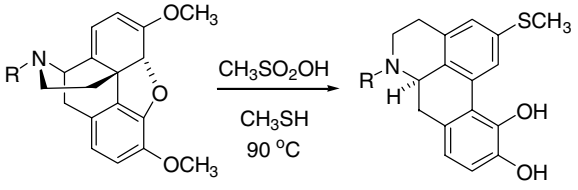
Synthesis and testing of a triaza-cyclopenta[*b*]phenanthrene scaffold as a DNA binding agent **pp 1902–1909**
Jaipal Hooda, David Bednarski, Lisa Irish and Steven M. Firestine*



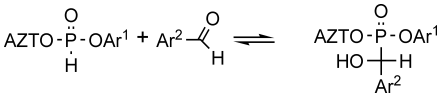
Synthesis, in vitro pharmacology and biodistribution studies of new PD 156707-derived ET_A receptor radioligands **pp 1910–1917**
Carsten Höltke,* Marilyn P. Law, Stefan Wagner, Hans-Jörg Breyholz, Klaus Kopka, Christoph Bremer, Bodo Levkau, Otmar Schober and Michael Schäfers



Synthesis and dopamine receptor binding of sulfur-containing aporphines **pp 1918–1923**
Miklós Tóth, Sándor Berényi, Csaba Csutorás,* Nora S. Kula, Kehong Zhang, Ross J. Baldessarini and John L. Neumeyer

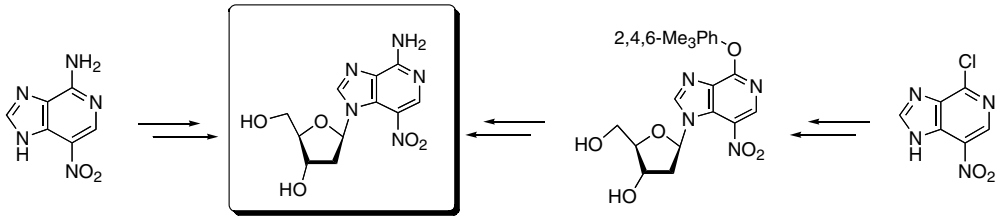


Aryl nucleoside *H*-phosphonates. Part 15: Synthesis, properties and, anti-HIV activity of aryl nucleoside 5′-α-hydroxyphosphonates **pp 1924–1934**
Agnieszka Szymańska, Marzena Szymczak, Jerzy Boryski, Jacek Stawiński, Adam Kraszewski,* Gabriella Collu, Giseppina Sanna, Gabriele Giliberti, Roberta Loddo and Paolo La Colla*



A series of aryl nucleoside α-hydroxylphosphonates was synthesised and evaluated as potential anti-HIV compounds. Their stability and decomposition paths in various media (including cell culture medium) can be controlled both by Ar^1 and Ar^2. These compounds showed high anti-HIV potency and in some cases considerably low cytotoxicity.

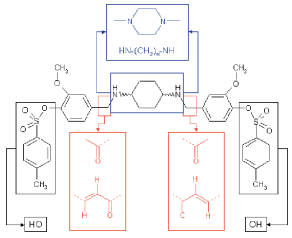
Synthesis of 3-deaza-3-nitro-2′-deoxyadenosine **pp 1935–1941**
Caroline Crey-Desbiolles and Mitsuharu Kotera*



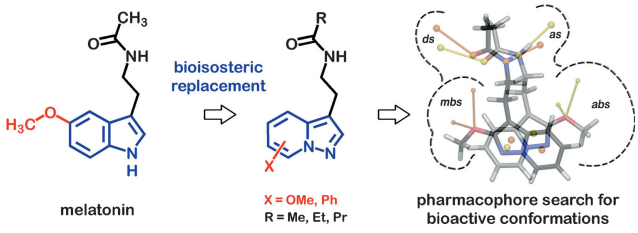
Deoxyadenosine mimicking photoactivable nitro nucleoside, 3-deaza-3-nitro-2′-deoxyadenosine, was synthesized.

Structural characteristics of novel symmetrical diaryl derivatives with nitrogenated functions. Requirements for cytotoxic activity **pp 1942–1948**
María Font,* Elena Ardaiz, Lucia Cordeu, Elena Cubedo, Jesús García-Foncillas, Carmen Sanmartin and Juan-Antonio Palop

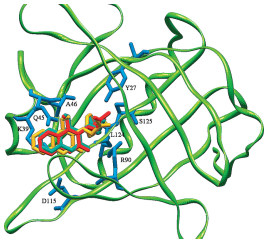
The variation in Log *P* and conformational behaviour in a series of symmetrical diaryl derivatives with nitrogenated functions has been studied by molecular modelling techniques. The data allow an initial separation of active and inactive compounds based on Log *P* values. In addition, it was observed that while the active compounds preferentially have an extended conformation, a certain type of folding takes place in inactive compounds.



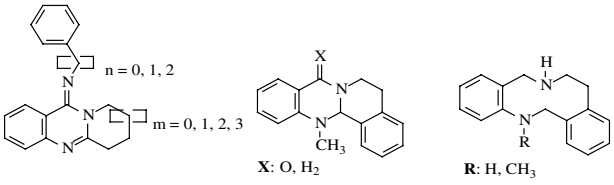
Bicyclic melatonin receptor agonists containing a ring-junction nitrogen: Synthesis, biological evaluation, and molecular modeling of the putative bioactive conformation **pp 1949–1958**
Jan Elsner, Frank Boeckler, Kathryn Davidson, David Sugden and Peter Gmeiner*



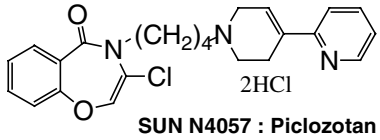
Selective binding of coumarin enantiomers to human α_1-acid glycoprotein genetic variants **pp 1959–1965**
Eszter Hazai,* Júlia Visy, Ilona Fitos, Zsolt Bikádi and Miklós Simonyi



Novel tricyclic quinazolinimines and related tetracyclic nitrogen bridgehead compounds as cholinesterase inhibitors with selectivity towards butyrylcholinesterase **pp 1966–1977**
Michael Decker,* Fabian Krauth and Jochen Lehmann



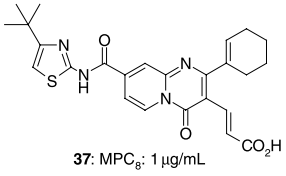
Synthesis, SAR studies, and evaluation of 1,4-benzoxazepine derivatives as selective 5-HT_{1A} receptor agonists with neuroprotective effect: Discovery of Piclozotan **pp 1978–1992**
Katsuhide Kamei,* Noriko Maeda, Kayoko Nomura, Makoto Shibata, Ryoko Katsuragi-Ogino, Makoto Koyama, Mika Nakajima, Teruyoshi Inoue, Tomochika Ohno and Toshio Tatsuoka



SUN N4057 : Piclozotan

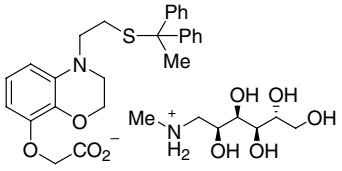
MexAB-OprM specific efflux pump inhibitors in *Pseudomonas aeruginosa*. Part 5: Carbon-substituted analogues at the C-2 position **pp 1993–2004**
Ken-ichi Yoshida,* Kiyoshi Nakayama, Noriko Kuru, Shozo Kobayashi, Masami Ohtsuka, Makoto Takemura, Kazuki Hoshino, Hiroko Kanda, Jason Z. Zhang, Ving J. Lee and William J. Watkins

A series of 2-carbon-substituted pyridopyrimidine derivatives were synthesized by palladium catalyzed cross-coupling reaction and evaluated for their ability to potentiate the activity of levofloxacin and aztreonam in *Pseudomonas aeruginosa*.



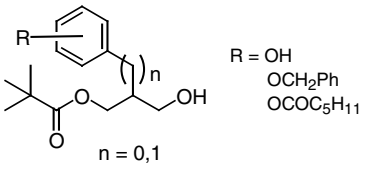
37: MPC_8: 1 μg/mL

Development of 3,4-dihydro-2*H*-benzo[1,4]oxazine derivatives as dual thromboxane A_2 receptor antagonists and prostacyclin receptor agonists **pp 2005–2021**
Michihiro Ohno,* Yoichiro Tanaka, Mitsuko Miyamoto, Takahiro Takeda, Kazuhiro Hoshi, Naohiro Yamada and Atsushi Ohtake

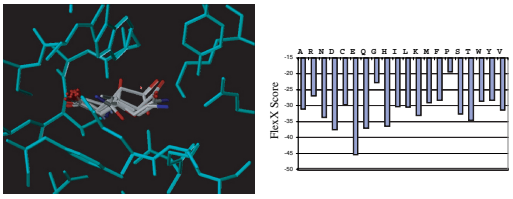


A novel series of 3,4-dihydro-2*H*-benzo[1,4]oxazin-8-yloxyacetic acid derivatives was discovered as potent dual-acting agents to block the thromboxane A_2 receptor and to activate prostacyclin receptor. Synthesis, structure–activity relationship, in vitro, ex vivo, and in vivo pharmacology of this series of compounds are described.

2-Benzyl and 2-phenyl-3-hydroxypropyl pivalates as protein kinase C ligands **pp 2022–2031**
Jeewoo Lee,* Ju-Hyun Lee, Su Yeon Kim, Nicholas A. Perry, Nancy E. Lewin, Jolene A. Ayres and Peter M. Blumberg



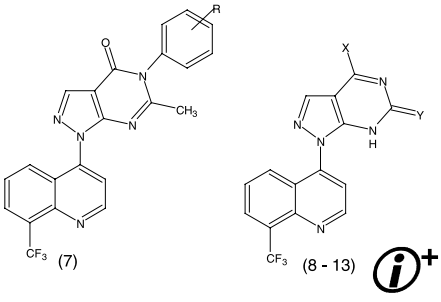
An evaluation of automated in silico ligand docking of amino acid ligands to Family C G-protein coupled receptors **pp 2032–2039**
Minghua Wang and David R. Hampson*



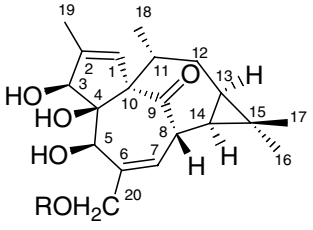
Amino acids docked into the binding pocket of mGluR1 and scored by FlexX.

Synthesis of some novel pyrazolo[3,4-*d*]pyrimidine derivatives as potential antimicrobial agents **pp 2040–2047**
Bantwal Shivarama Holla,* Manjathuru Mahalinga, Mari Sitambaram Karthikeyan, Padiyath Mohamed Akberali and Nalilu Sucheta Shetty

A series of pyrazolo[3,4-*d*] pyrimidine nucleus containing 8-(trifluoromethyl)quinoline have been synthesized. The synthesis of this ring system has been accomplished from two pyrazole intermediates, 5-amino-1-[8-(trifluoromethyl)quinolin-4-yl]-1*H*-pyrazole-4-carboxylate and 5-amino-1-[8-(trifluoromethyl)quinolin-4-yl]-1*H*-pyrazole-4-carbonitrile. The antimicrobial activity study of the newly synthesized pyrazolo[3,4-*d*] pyrimidine ring system is discussed.

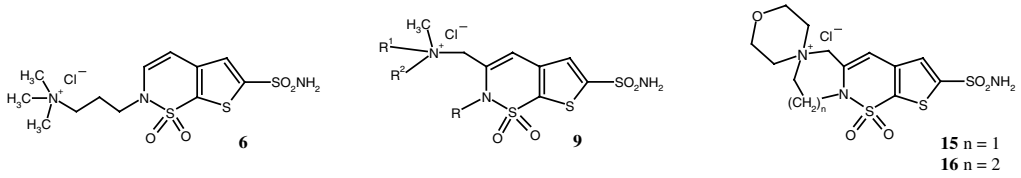


Inhibition of cellular proliferation by diterpenes, topoisomerase II inhibitor **pp 2048–2051**
Shohei Miyata,* Li-Yan Wang, Chisato Yoshida and Susumu Kitanaka

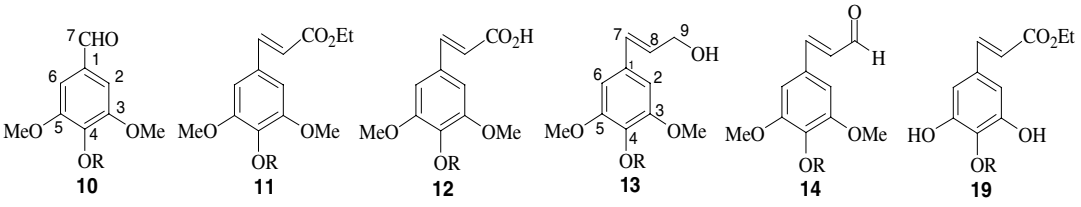


We selected terpene compounds having capacities for inhibition of cellular proliferation and topoisomerase II activity by useful inhibition assay method of proliferation using isolated embryonic cells of *Xenopus*.

Quaternary ammonium substituted thieno[3,2-*e*]-1,2-thiazine-6-sulfonamide 1,1-dioxides: Potential membrane-impermeable inhibitors of carbonic anhydrase **pp 2052–2059**
Jesse A. May,* Abdelmoula Namil, Hwang-Hsing Chen, Anura P. Dantanarayana, Brian Dupré and John C. Liao



Design, synthesis, and SAR analysis of cytotoxic sinapyl alcohol derivatives **pp 2060–2071**
Hong Bin Zou, Sheng Yi Dong, Chang Xin Zhou, Li Hong Hu, Yi Hang Wu, Hai Bo Li, Jing Xu Gong, Lian Li Sun, Xiu Mei Wu, Hua Bai, Bo Tao Fan, Xiao Jiang Hao, Joachim Stöckigt and Yu Zhao*



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*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

2006: The cover figure shows a synthetic multifunctional pore that is composed of rigid-rod staves (para-octiphenyls, tan) and beta-sheet hoops (arrows) and can be activated with external ligands (fullerenes, golden spheres) and closed with internal blockers (alpha-helix, red ribbon) [Gorteau, V.; Bollot, G.; Mareda, J.; Pasini, D.; Tran, D.-H.; Lazar, A. N.; Coleman, A. W.; Sakai, N.; Matile, S. *Bioorg. Med. Chem.* **2005**, *13*, 5171–5180].

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ISSN 0968-0896