

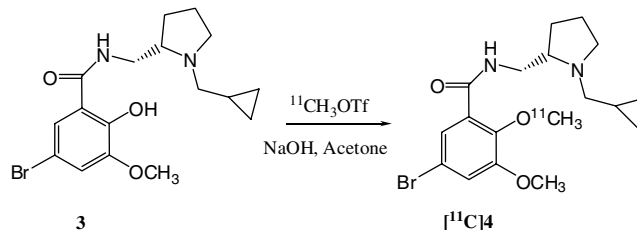
Contents

ARTICLES

[¹¹C]Cyclopropyl-FLB 457: A PET radioligand for low densities of dopamine D₂ receptors

pp 6467–6473

Anu J. Airaksinen*, Sangram Nag, Sjoerd J. Finnema, Jogeshwar Mukherjee, Sankha Chattopadhyay, Balázs Gulyás, Lars Farde, Christer Halldin

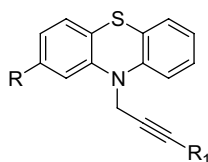


The ¹¹C labelled (S)-5-bromo-N-[(1-cyclopropylmethyl-2-pyrrolidinyl)methyl]-2,3-dimethoxybenzamide ([¹¹C]4) was synthesized and its dopamine D₂/D₃ receptor binding was evaluated in post-mortem human brain autoradiography and with PET in cynomolgus monkeys.

Multidrug resistance reverting activity and antitumor profile of new phenothiazine derivatives

pp 6474–6482

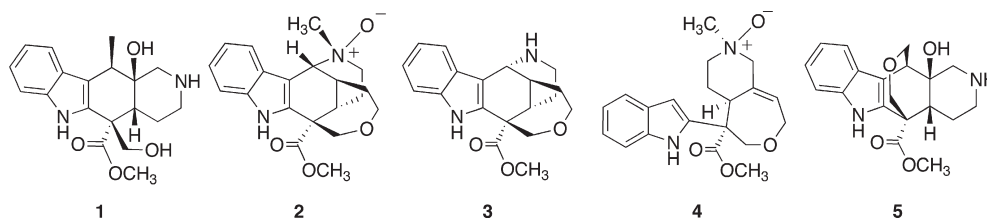
Alessandra Bisi*, Maria Meli, Silvia Gobbi, Angela Rampa, Manlio Tolomeo, Luisa Dusonchet*



Alstilobanines A–E, new indole alkaloids from *Alstonia angustiloba*

pp 6483–6488

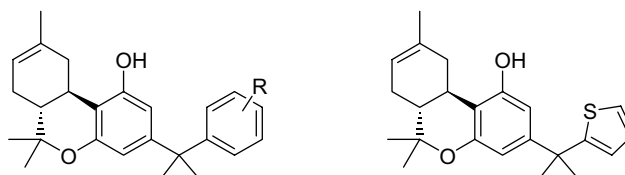
Koichiro Koyama, Yusuke Hirasawa, Kazumasa Zaima, Teh Chin Hoe, Kit-Lam Chan, Hiroshi Morita*



Exploring the substituent effects on a novel series of C1'-dimethyl-aryl Δ^8 -tetrahydrocannabinol analogs

pp 6489–6500

Mathangi Krishnamurthy, Steven Gurley, Bob M. Moore II*

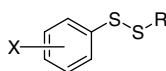


R = halo, alkyl, nitrile, or acetamino

Unsymmetric aryl-alkyl disulfide growth inhibitors of methicillin-resistant *Staphylococcus aureus* and *Bacillus anthracis*

pp 6501–6508

Edward Turos*, Kevin D. Revell, Praveen Ramaraju, Danielle A. Gergeres, Kerriann Greenhalgh, Ashley Young, Nalini Sathyanarayan, Sonja Dickey, Daniel Lim, Mamoun M. Alhamadsheh, Kevin Reynolds

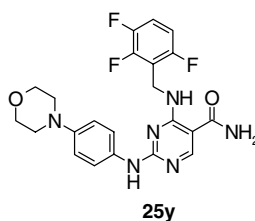


A series of aryl-alkyl disulfides have been identified to have strong antibacterial activity against *Staphylococcus aureus* (including MRSA) and *Bacillus anthracis*, and act as inhibitors of fatty acid biosynthesis FabH protein.

Identification of 4-benzylamino-2-[(4-morpholin-4-ylphenyl)amino]pyrimidine-5-carboxamide derivatives as potent and orally bioavailable STAT6 inhibitors

pp 6509–6521

Shinya Nagashima*, Hiroshi Nagata, Masahiro Iwata, Masaki Yokota, Hiroyuki Moritomo, Masaya Orita, Sadao Kuromitsu, Akiko Koakutsu, Keiko Ohga, Makoto Takeuchi, Mitsuki Ohta, Shin-ichi Tsukamoto

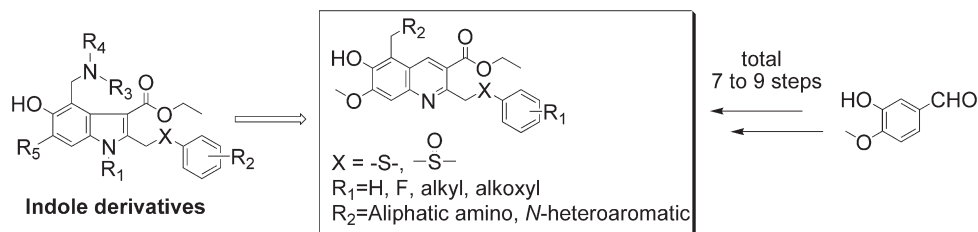


The novel 4-benzylamino-2-[(4-morpholin-4-ylphenyl)amino]pyrimidine-5-carboxamide derivative **25y** (YM-341619, AS1617612) potently inhibited STAT6 activation and Th2 differentiation with IC_{50} values of 0.70 and 0.28 nM, respectively, and showed an oral bioavailability of 25% in mouse.

Synthesis and anti-hepatitis B virus evaluation of novel ethyl 6-hydroxyquinoline-3-carboxylates in vitro

pp 6522–6527

Yajing Liu, Yanfang Zhao, Xin Zhai, Xusheng Feng, Jinxin Wang, Ping Gong*

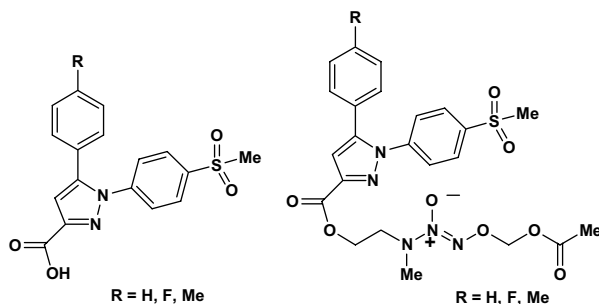


A series of novel ethyl 6-hydroxyquinoline-3-carboxylates were designed and synthesized, and their inhibitory activities against hepatitis B virus (HBV) were compared to that of lamivudine in HepG2.2.15 cells.

Diazen-1-ium-1,2-diolated nitric oxide donor ester prodrugs of 1-(4-methanesulfonylphenyl)-5-aryl-1H-pyrazol-3-carboxylic acids: Synthesis, nitric oxide release studies and anti-inflammatory activities

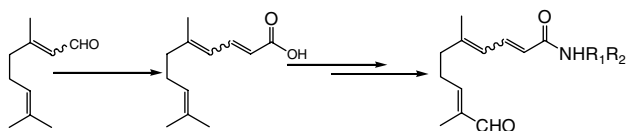
pp 6528–6534

Khaled R.A. Abdellatif, Morshed Alam Chowdhury, Ying Dong, Edward E. Knaus*

**Citral derived amides as potent bacterial NorA efflux pump inhibitors**

pp 6535–6543

Niranjan Thota, Surrinder Koul*, Mallepally V. Reddy, Payare L. Sangwan, Inshad A. Khan, Ashwani Kumar, Alsaba F. Raja, Samar S. Andotra, Ghulam N. Qazi



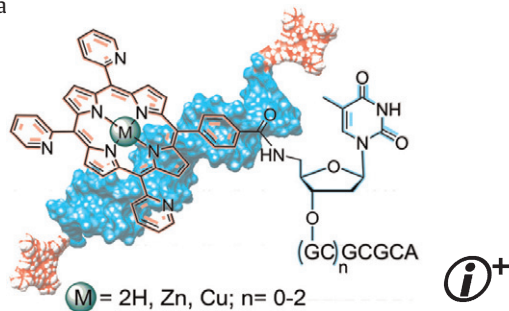
Potent amides as efflux pump inhibitors targeting NorA system of *Staphylococcus aureus* have been prepared from citral and citronellal and shown to possess better potentiating activity than known EPIs.

Synthesis and characterization of water-soluble free-base, zinc and copper porphyrin–oligonucleotide conjugates

pp 6544–6551

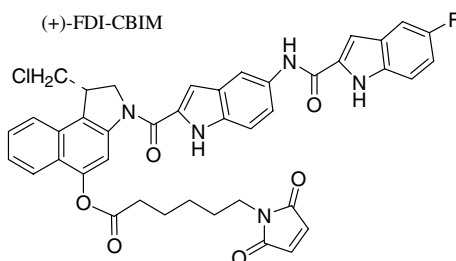
Angela Mammana, Tomohiro Asakawa, Klaus Bitsch-Jensen, Amanda Wolfe, Saireudee Chaturantabut, Yuko Otani, Xiaoxu Li, Zengmin Li, Koji Nakanishi, Milan Balaz*, George A. Ellestad*, Nina Berova*

End-capped 5'-porphyrin- and 5'-metalloporphyrin-DNA conjugates have been synthesized. Spectroscopic and HPLC properties of all conjugates have been studied. Unexpected partial metallation of free-base porphyrin-DNA conjugates has been observed during the DNA cleavage and deprotection.

**Synthesis and antitumor activity evaluations of albumin-binding prodrugs of CC-1065 analog**

pp 6552–6559

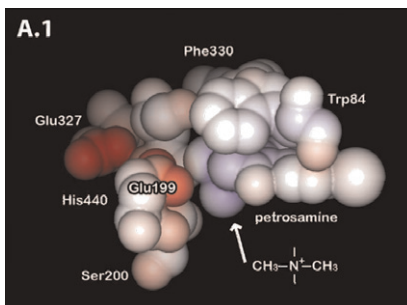
Yuqiang Wang*, Jie Jiang, Xiaojian Jiang, Shaohui Cai, Hai Han, Lianfa Li, Zhiming Tian, Wei Jiang, Zaijun Zhang, Ying Xiao, Susan C. Wright, James W. Larrick



Petrosamine, a potent anticholinesterase pyridoacridine alkaloid from a Thai marine sponge *Petrosia* n. sp.

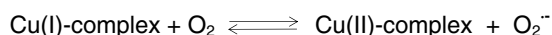
pp 6560–6567

Veena S. Nukoolkarn, Suwipa Saen-oon, Thanyada Rungrotmongkol, Supot Hannongbua, Kornkanok Ingkaninan, Khanit Suwanborirux*

**Cu(I)–Glutathione complex: A potential source of superoxide radicals generation**

pp 6568–6574

Hernán Speisky*, Maritza Gómez, Catalina Carrasco-Pozo, Edgar Pastene, Camilo Lopez-Alarcón, Claudio Olea-Azar

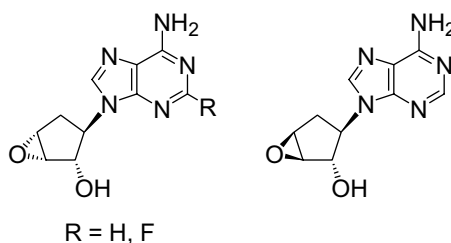


Cu^{2+} and GSH molecules react swiftly to form a Cu(I)–glutathione complex. First time evidence is presented showing the ability of such complex to reduce molecular oxygen into superoxide radicals.

Synthesis of 3',4'-epoxynoraristeromycin analogs for molecular labeling probe of S-adenosyl-L-homocysteine hydrolase

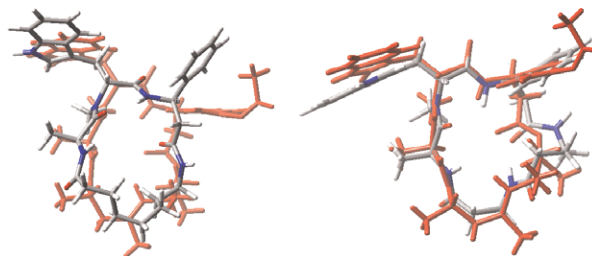
pp 6575–6579

Hiroharu Kojima, Atsushi Kozaki, Masafumi Iwata, Takayuki Ando, Yukio Kitade*

**Synthetic and pharmacological studies on new simplified analogues of the potent actin-targeting Jaspamide**

pp 6580–6588

Stefania Terracciano, Ines Bruno*, Elisabetta D'Amico, Giuseppe Bifulco, Angela Zampella, Valentina Sepe, Charles D. Smith, Raffaele Riccio

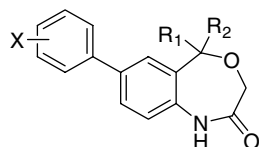


A new collection of simplified analogues of the actin-binding natural cyclodepsipeptide Jaspamide was designed and synthesized. The macrocycle closure has been accomplished through classic peptide bond formation or microwave supported RCM reaction.

7-Aryl 1,5-dihydro-benzo[e][1,4]oxazepin-2-ones and analogs as non-steroidal progesterone receptor antagonists

pp 6589–6600

Puwen Zhang*, Jeffrey C. Kern, Eugene A. Terefenko, Andrew Fensome, Ray Unwalla, Zhiming Zhang, Jeffrey Cohen, Thomas J. Berrodin, Matthew R. Yudt, Richard C. Winneker, Jay Wrobel



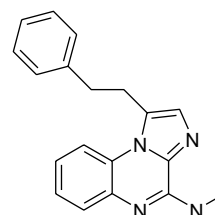
A series of novel 7-aryl benzo[1,4]oxazepin-2-ones were evaluated as progesterone receptor (PR) modulators. Several analogs were potent PR antagonists and active in the rat uterine decidualization model at 3 mg/kg when dosed orally.

In vitro and in vivo anti-tumoral activities of imidazo[1,2-a]quinoxaline, imidazo[1,5-a]quinoxaline, and pyrazolo[1,5-a]quinoxaline derivatives

pp 6601–6610

Georges Moarbess, Carine Deleuze-Masquefa*, Vanessa Bonnard, Stéphanie Gayraud-Paniagua, Jean-Rémi Vidal, Françoise Bressolle, Frédéric Pinguet, Pierre-Antoine Bonnet

EAPB0203 bearing phenethyl as substituent at position 1 and methylamine at position 4 showed the highest activity on human melanoma cell lines compared to fotemustine and imiquimod used as references. In vivo, **EAPB0203** treatment schedules caused a significant decrease in tumor size compared to vehicle control and fotemustine treatments.

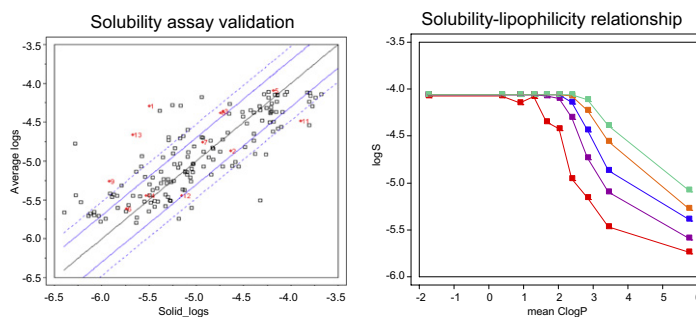


EAPB0203
IC₅₀ = 1.57 ± 0.56 μM

**High throughput solubility determination with application to selection of compounds for fragment screening**

pp 6611–6616

Nicola Colclough, Alison Hunter, Peter W. Kenny*, Rod S. Kittlety, Lynsey Lobedan, Kin Y. Tam*, Mark A. Timms

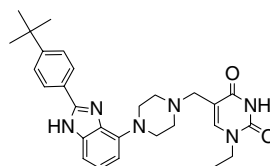
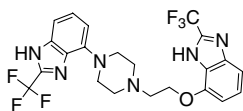
**2-Phenyl-4-piperazinylbenzimidazoles: Orally active inhibitors of the gonadotropin releasing hormone (GnRH) receptor**

pp 6617–6640

Jeffrey C. Pelletier*, Murty Chengalvala, Josh Cottom, Irene Feingold, Lloyd Garrick, Daniel Green, Diane Hauze, Christine Huselton, James Jetter, Wenling Kao, Gregory S. Kopf, Joseph T. Lundquist IV, Charles Mann, John Mehlmann, John Rogers, Linda Shanno, Jay Wrobel

Screening lead

hGnRH binding
IC₅₀ = 1540 nM



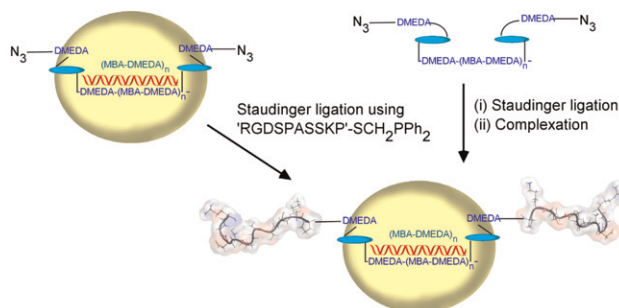
Orally active

hGnRH binding
IC₅₀ = 1.7 nM

Targeting of polyamidoamine–DNA nanoparticles using the Staudinger ligation: Attachment of an RGD motif either before or after complexation

pp 6641–6650

Susan M. Parkhouse, Martin C. Garnett, Weng C. Chan*



OTHER CONTENTS

Instructions to contributors

p I

*Corresponding author

+ Supplementary data available via ScienceDirect

COVER

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

Available online at

ScienceDirect
www.sciencedirect.com

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



ISSN 0968-0896