



Bioorganic & Medicinal Chemistry Volume 19, Issue 3, 2011

Symposium-in-Print

Imaging Probes

Edited by:

Dr. Carsten Schultz

Interdisciplinary Group Leader and Senior Scientist, EMBL Heidelberg, Schultz Group, MeyerhofstraÙ 1, 69117 Heidelberg, Germany

Dr. Silvio Aime

Department of Chemistry IFM and Molecular Imaging Center, University of Torino, Via Nizza 52, Torino, Italy

Contents

SPECIAL ISSUE ARTICLES

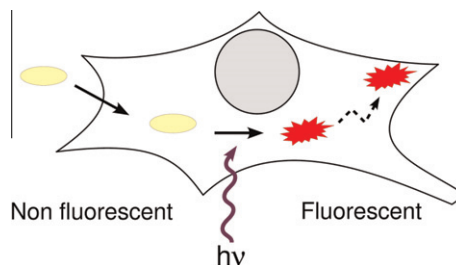
Editorial

Small photoactivatable molecules for controlled fluorescence activation in living cells

David Puliti, David Warther, Clelia Orange, Alexandre Specht, Maurice Goeldner*

p 1022

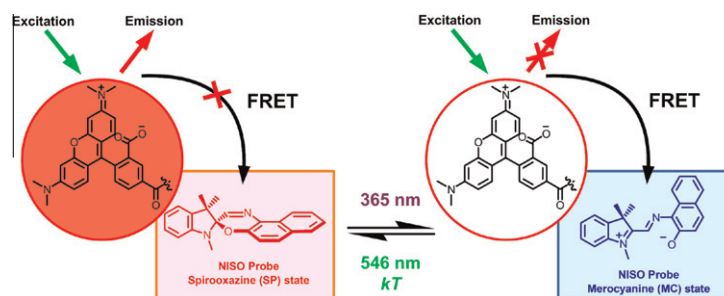
pp 1023–1029



Rational design, synthesis, and characterization of highly fluorescent optical switches for high-contrast optical lock-in detection (OLID) imaging microscopy in living cells

Chutima Petchprayoon, Yuling Yan, Shu Mao, Gerard Marriott*

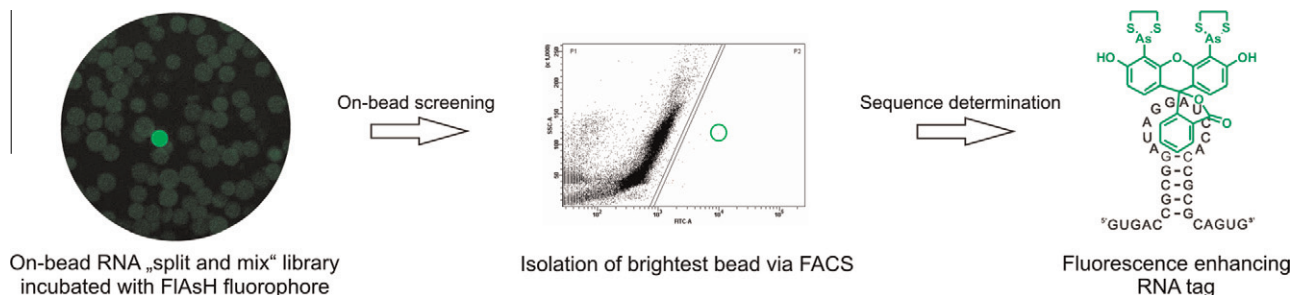
pp 1030–1040



Isolation and characterization of fluorescence-enhancing RNA tags

pp 1041–1047

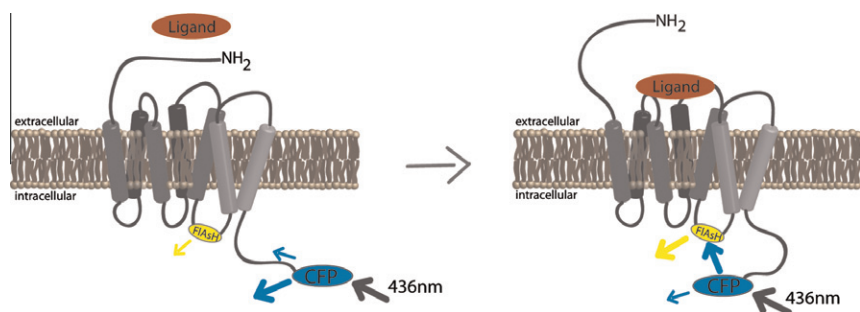
Anna Wiesmayr, Andres Jäschke*



FRET-based sensors for the human M₁-, M₃-, and M₅-acetylcholine receptors

pp 1048–1054

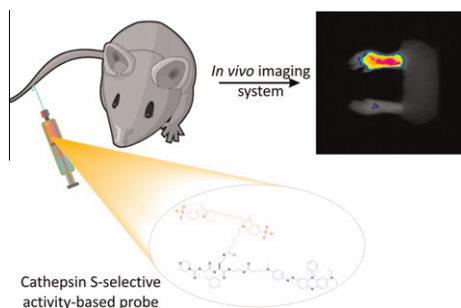
Nicole Ziegler, Julia Bätz, Ulrike Zabel, Martin J. Lohse, Carsten Hoffmann*



Functional in vivo imaging of cysteine cathepsin activity in murine model of inflammation

pp 1055–1061

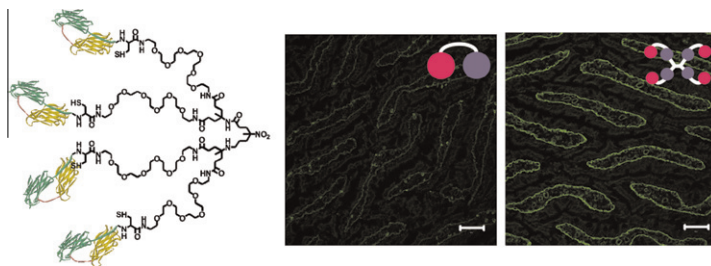
Dejan Caglič, Anja Globisch, Maik Kindermann, Ngee-Han Lim, Volker Jeske, Hans-Paul Juretschke, Eckart Bartnik, K. Ulrich Weithmann, Hideaki Nagase, Boris Turk, K. Ulrich Wendt*



Collagen targeting using multivalent protein-functionalized dendrimers

pp 1062–1071

Monica Breurken, Edith H. M. Lempens, Rinske P. Temming, Brett A. Helms, E. W. Meijer, Maarten Merckx*



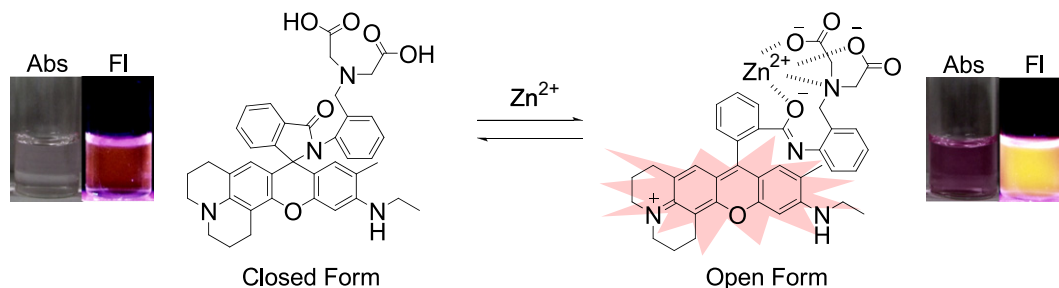
Strength in numbers: semi-synthetic multivalent collagen binding proteins were obtained by native chemical ligation of CNA35-thioesters and cysteine-functionalized divalent (AB₂) and tetravalent (AB₄) dendritic wedges.



Design and synthesis of a novel fluorescence probe for Zn²⁺ based on the spirolactam ring-opening process of rhodamine derivatives

pp 1072–1078

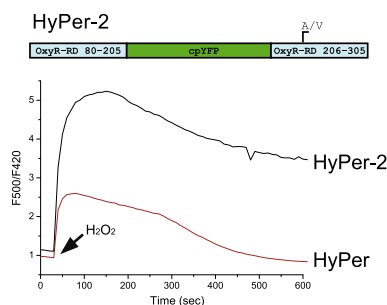
Hiromi Sasaki, Kenjiro Hanaoka, Yasuteru Urano, Takuya Terai, Tetsuo Nagano*



A genetically encoded sensor for H₂O₂ with expanded dynamic range

pp 1079–1084

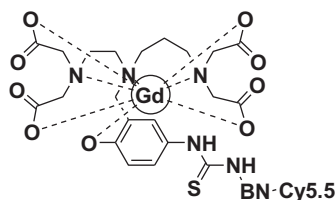
Kseniya N. Markvicheva, Dmitry S. Bilan, Natalia M. Mishina, Andrey Yu. Gorokhovatsky, Leonid M. Vinokurov, Sergey Lukyanov, Vsevolod V. Belousov*

Single point mutation in OxyR-RD part of the HyPer biosensor cause increase of the dynamic range of the probe responding to H₂O₂.

In vivo MR/optical imaging for gastrin releasing peptide receptor of prostate cancer tumor using Gd-TTDA-NP-BN-Cy5.5

pp 1085–1096

Ying-Hsiu Lin, Kasala Dayananda, Chiao-Yun Chen, Gin-Chung Liu, Tsai-Yueh Luo, Hui-Sheng Hsu, Yun-Ming Wang*

Bombesin analogue (BN) = Lys-Gly-Gly-Gly-Gln-Trp-Ala-Val-Gly-His-Leu-Met-NH₂

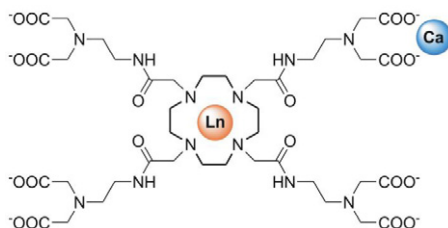
This article reports the synthesis, in vitro, and in vivo studies of Gd-TTDA-NP-BN-Cy5.5 as a new dual contrast agent for MR/Optical imaging of gastrin releasing peptide receptor in prostate cancer tumor.



Calcium-responsive paramagnetic CEST agents

pp 1097–1105

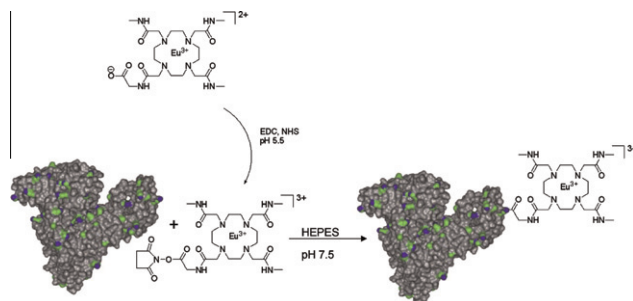
Goran Angelovski*, Thomas Chauvin, Rolf Pohmann, Nikos K. Logothetis, Éva Tóth*

The investigated tetraamide Yb³⁺ and Eu³⁺ complexes exhibit a marked alteration in their chemical exchange saturation transfer (CEST) properties upon Ca²⁺ binding which can be exploited for the MRI detection of Ca²⁺ concentration changes.

Strategies for labeling proteins with PARACEST agents

pp 1106–1114

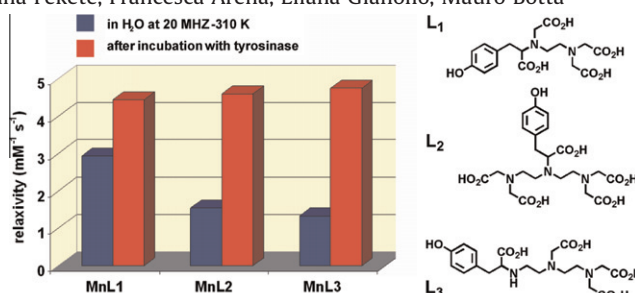
Olga Vasalatiy, Piyu Zhao, Mark Woods, Andrei Marconescu, Aminta Castillo-Muzquiz, Philip Thorpe, Garry E. Kiefer, A. Dean Sherry*



Responsive Mn(II) complexes for potential applications in diagnostic Magnetic Resonance Imaging

pp 1115–1122

Gabriele A. Rolla, Lorenzo Tei, Marianna Fekete, Francesca Arena, Eliana Gianolio, Mauro Botta*



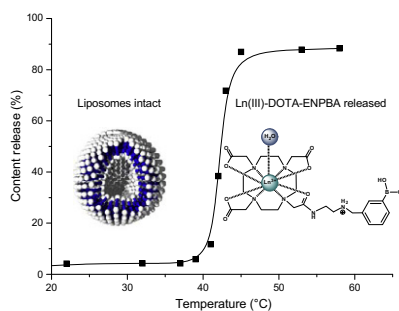
This paper reports on the synthesis and in vitro evaluation of three novel Mn(II) complexes as potential MRI probes for the enzyme tyrosinase to be used in the diagnosis of melanoma cancer.



Development of a liposomal delivery system for temperature-triggered release of a tumor targeting agent, Ln(III)-DOTA-phenylboronate

pp 1123–1130

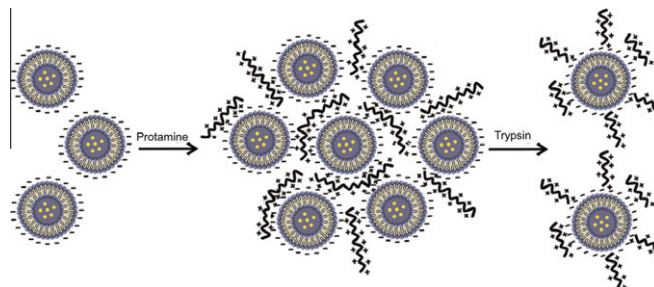
Kristina Djanashvili*, Timo L. M. ten Hagen, Roy Blangé, Debby Schipper, Joop A. Peters, Gerben A. Koning*



Supramolecular protamine/Gd-loaded liposomes adducts as relaxometric protease responsive probes

pp 1131–1135

Sara Figueiredo, João Nuno Moreira, Carlos F. G. C. Geraldes, Silvio Aime, Enzo Terreno*



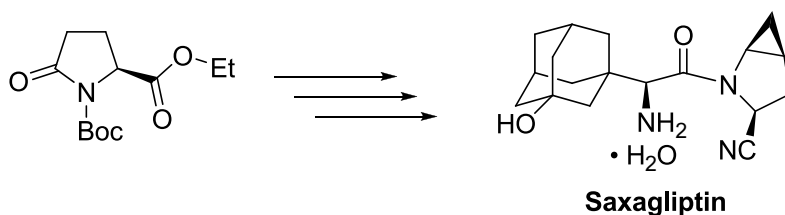
A new approach to enzyme-responsive MRI agents is presented based on the relaxivity enhancement caused by the disruption of aggregates formed by liposomes and a macromolecular substrate cleaved by the enzyme.

REVIEW

Synthetic approaches to the 2009 new drugs

pp 1136–1154

Kevin K.-C. Liu, Subas M. Sakya, Christopher J. O'Donnell*, Andrew C. Flick, Jin Li



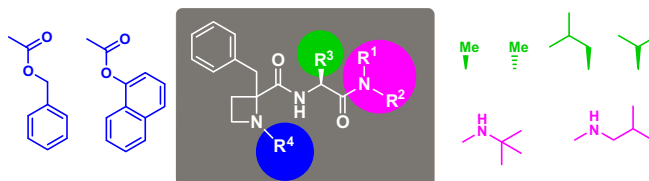
Plus the 20 other New Drugs marketed in 2009

REGULAR ARTICLES

Synthesis and SAR studies on azetidine-containing dipeptides as HCMV inhibitors

pp 1155–1161

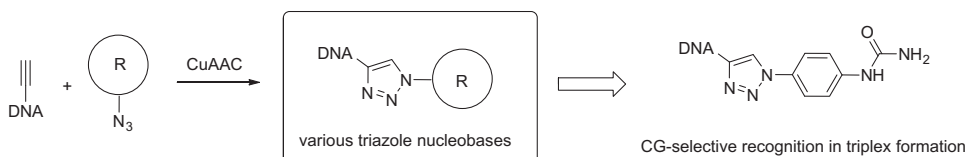
Paula Pérez-Faginas, M. Teresa Aranda, M. Teresa García-López, Robert Snoeck, Graciela Andrei, Jan Balzarini, Rosario González-Muñiz*



Synthesis and triplex-forming ability of oligonucleotides bearing 1-substituted 1H-1,2,3-triazole nucleobases

pp 1162–1166

Yoshiyuki Hari*, Motoi Nakahara, Juanjuan Pang, Masaaki Akabane, Takeshi Kuboyama, Satoshi Obika*

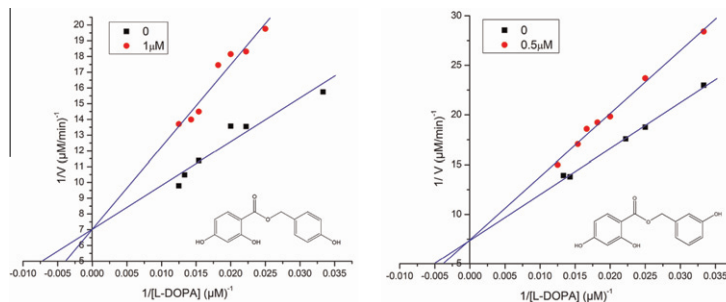


Benzyl benzoates: New phlorizin analogs as mushroom tyrosinase inhibitors

pp 1167–1171

Yuntai Fang, Yaozong Chen, Guanfeng Feng, Lin Ma*

Fourteen Benzyl benzoates with hydroxyl(s) (**3–16**) were synthesised and their inhibitory activity on mushroom tyrosinase were tested. Results indicated that five among these 14 compounds exhibited an IC_{50} value less than 10 μM , while 4-hydroxybenzyl 2,4-dihydroxybenzoate (**5**), got the best inhibitory activity. Further studies showed these five compounds were competitive inhibitors of tyrosinase.



A new β -carbonic anhydrase from *Brucella suis*, its cloning, characterization, and inhibition with sulfonamides and sulfamates, leading to impaired pathogen growth

pp 1172–1178

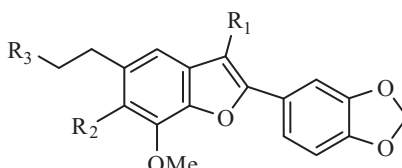
Pascale Joseph, Safia Ouahrani-Bettache, Jean-Louis Montero, Isao Nishimori, Tomoko Minakuchi, Daniela Vullo, Andrea Scozzafava, Jean-Yves Winum*, Stephan Köhler*, Claudiu T. Supuran*



Synthesis of egonol derivatives and their antimicrobial activities

pp 1179–1188

Safiye Emirdağ-Öztürk*, Tamer Karayildirim, Hüseyin Anil



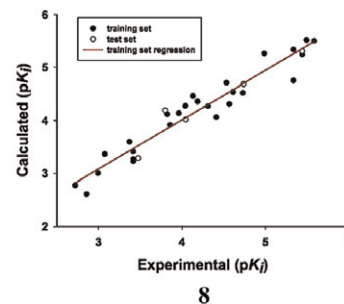
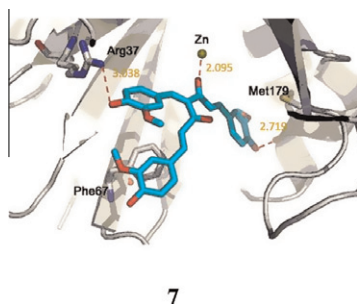
Eighteen egonol derivatives via substitution, (at C-3, C-6, and C-3''), oxidation, reduction and condensation reactions were synthesized and their antimicrobial activities against four well-known bacteria and yeast were investigated.

Identification of curcumin derivatives as human glyoxalase I inhibitors: A combination of biological evaluation, molecular docking, 3D-QSAR and molecular dynamics simulation studies

pp 1189–1196

Minggui Yuan, Minxian Luo, Yao Song, Qiu Xu, Xiaofeng Wang, Yi Cao, Xianzhang Bu*, Yanliang Ren*, Xiaopeng Hu

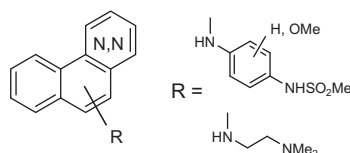
We designed, synthesized and tested a series of curcumin derivatives possessing high inhibitory activity against human GLO I, the binding model for compound **8** was obtained by MD simulations, as shown in Figure 7. The satisfactory correlation of pK_i value between experiment and theory was shown in Figure 8.



Benzoquinazoline derivatives as new agents affecting DNA processing

pp 1197–1204

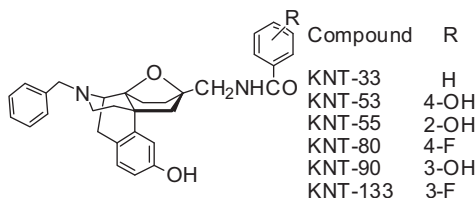
Giovanni Marzaro, Lisa Dalla Via, Antonio Toninello, Adriano Guiotto, Adriana Chilin*



Synthesis of 6,14-epoxymorphinan derivatives and their pharmacologies

pp 1205–1221

Toru Nemoto, Naoshi Yamamoto, Akio Watanabe, Hideaki Fujii, Ko Hasebe, Mayumi Nakajima, Hidenori Mochizuki, Hiroshi Nagase*

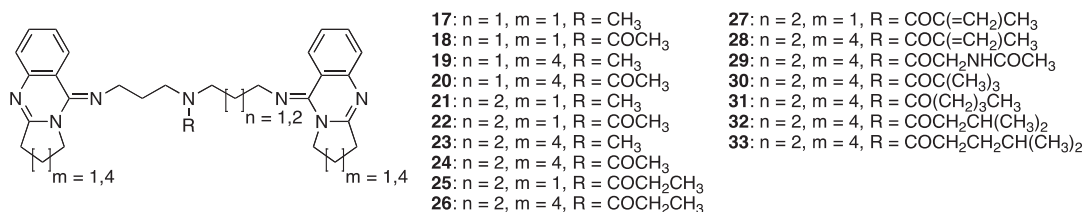


We found that 17-benzyl-6,14-epoxymorphinan derivatives showed high selectivities for the opioid κ receptor. The 17-benzyl substituent may play an important role for developing κ selectivity.

Probing the mid-gorge of cholinesterases with spacer-modified bivalent quinazolinimines leads to highly potent and selective butyrylcholinesterase inhibitors

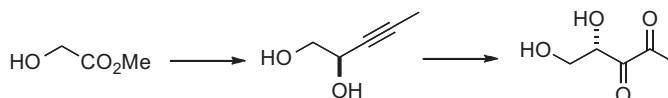
pp 1222–1235

Xinyu Chen, Irina G. Tikhonova, Michael Decker*

**An efficient synthesis of the precursor of AI-2, the signalling molecule for inter-species quorum sensing**

pp 1236–1241

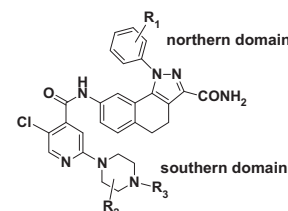
Osvaldo S. Ascenso, João C. Marques, Ana Rita Santos, Karina B. Xavier, M. Rita Ventura, Christopher D. Maycock*

**Aminopyridinecarboxamide-based inhaled IKK-2 inhibitors for asthma and COPD: Structure–activity relationship**

pp 1242–1255

Jin Xie*, Gennadiy I. Poda, Yiding Hu, Natalie X. Chen, Richard F. Heier, Serge G. Wolfson, Matthew T. Reding, Patrick J. Lennon, Ravi G. Kurumbail, Shaun R. Selness, Xiong Li, Nandini N. Kishore, Cynthia D. Sommers, Lori Christine, Sheri L. Bonar, Neetu Venkatraman, Sumathy Mathialagan, Sarah J. Brustkern, Horng-Chih Huang*

Installation of sites for metabolism in the lead compound **PHA-767408** was the key focus of the IKK-2 inhaled program. This paper reports our efforts to identify a novel series of aminopyridinecarboxamide-based IKK-2 inhibitors which display low nanomolar potency against IKK-2 with long duration of action (DOA) and metabolically labile with potential capability for multiple routes of clearance. Several lead compounds have demonstrated their potential usefulness in the treatment of asthma and chronic obstructive pulmonary disease (COPD).

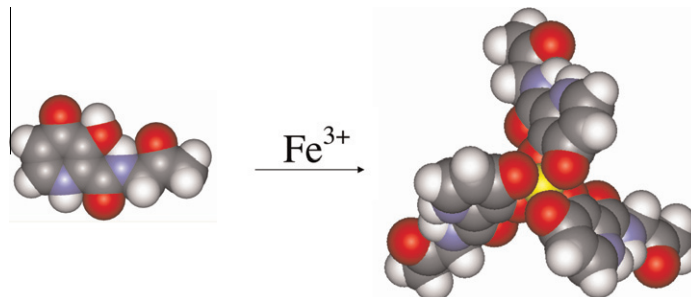


Synthesis, physical–chemical characterisation and biological evaluation of novel 2-amido-3-hydroxypyridin-4(1*H*)-ones: Iron chelators with the potential for treating Alzheimer's disease

pp 1285–1297

Alessandra Gaeta, Francisco Molina-Holgado, Xiao L. Kong, Sarah Salvage, Sarah Fakih, Paul T. Francis, Robert J. Williams, Robert C. Hider*

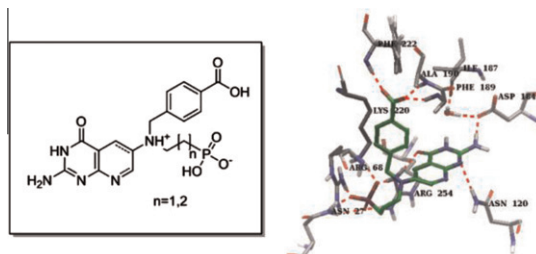
Peptide substituents at the 2-position of pyridine-4-ones minimise enzyme inhibitory properties without influencing iron scavenging ability.



Synthesis of bi-substrate state mimics of dihydropteroate synthase as potential inhibitors and molecular probes

pp 1298–1305

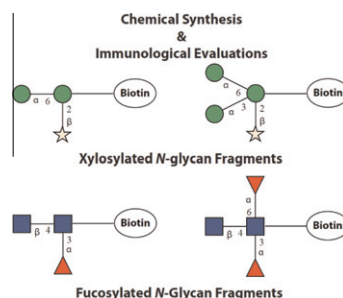
Jianjun Qi, Kristopher G. Virga, Sourav Das, Ying Zhao, Mi-Kyung Yun, Stephen W. White, Richard E. Lee*



Synthesis of cross-reactive carbohydrate determinants fragments as tools for in vitro allergy diagnosis

pp 1306–1320

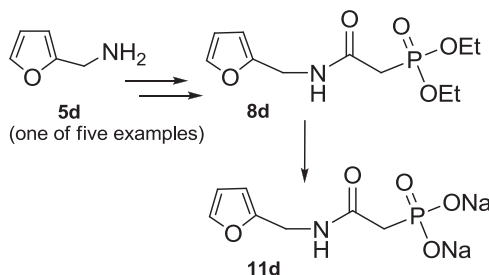
Mayeul Collot, Iain B. H. Wilson, Merima Bublin, Karin Hoffmann-Sommergruber, Jean-Maurice Mallet*



Synthesis and evaluation of phosphonated *N*-heteroarylcarboxamides as DOXP-reductoisomerase (DXR) inhibitors

pp 1321–1327

Taryn Bodill, Anne C. Conibear, Gregory L. Blatch, Kevin A. Lobb, Perry T. Kaye*



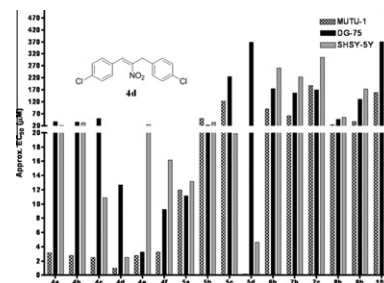
Esters and disodium salts of various heteroarylcarbamoylphosphonic acids have been prepared and evaluated as potential DXR inhibitors, using in silico docking studies, STD NMR analysis and enzymes inhibition assays.



Synthesis and serotonin transporter activity of 1,3-bis(aryl)-2-nitro-1-propenes as a new class of anticancer agents pp 1328–1348

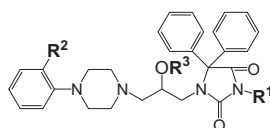
Yvonne M. McNamara, Suzanne M. Cloonan, Andrew J. S. Knox, John J. Keating, Stephen G. Butler, Günther H. Peters, Mary J. Meegan, D. Clive Williams*

A series of 1,3-bis(aryl)-2-nitro-1-propenes exhibit a selective, potent antiproliferative effect on Burkitt's lymphoma cell lines, independently of their serotonin transporter (SERT) activities.



Pharmacophore models based studies on the affinity and selectivity toward 5-HT_{1A} with reference to α_1 -adrenergic receptors among arylpiperazine derivatives of phenytoin pp 1349–1360

Jadwiga Handzlik, Ewa Szymańska, Krystyna Nędza, Monika Kubacka, Agata Siwek, Szczepan Mogilski, Jarosław Handzlik, Barbara Filipek, Katarzyna Kieć-Kononowicz*

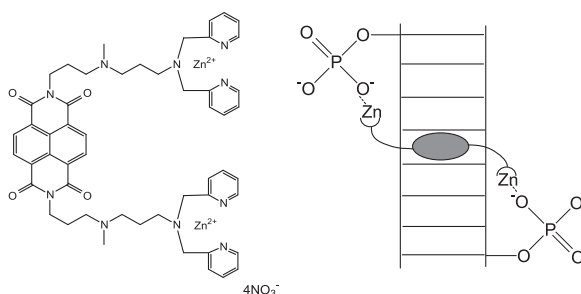


5-HT_{1A}/ α_1 -adrenoceptors affinity and selectivity of 1-[2-hydroxy-3-(4-phenylpiperazin-1-yl)-propyl]-2,4-dioxo-5,5-diphenylimidazolidine derivatives are described. Synthesis, molecular modelling, radioligand binding assays, functional bioassays and SAR-studies were carried out.



Discrimination of phosphorylated double stranded DNA by naphthalene diimide having zinc(II) dipicolylamine complexes pp 1361–1365

Sadayoshi Watanabe, Keiichi Ohtsuka, Shinobu Sato, Shigeori Takenaka*



OTHER CONTENTS

Corrigenda

pp 1366–1367

Bioorganic & Medicinal Chemistry Reviews and Perspectives

pp I–III

*Corresponding author

Supplementary data available via ScienceDirect

COVER

The cover graphic features three imaging probe examples: a gadolinium complex used as contrast agent in magnetic resonance imaging (MRI) of patients, a FRET reporter to measure phospholipase A2 activity in living cells, and Fura-2, a calcium sensor developed by Roger Tsien's group in the eighties that revolutionized cell biology to become a more quantitative and molecular discipline.

Available online at 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. Also covered in the abstract and citation database SCOPUS®. Full text available on ScienceDirect®



ISSN 0968-0896