ELSEVIER

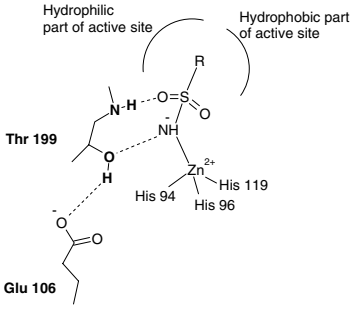
Bioorganic &
Medicinal
Chemistry

Bioorganic & Medicinal Chemistry Vol. 15, No. 13, 2007

# Contents

## REVIEW

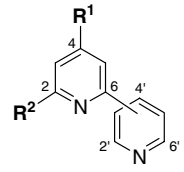
**Carbonic anhydrases as targets for medicinal chemistry** **pp 4336–4350**
Claudiu T. Supuran* and Andrea Scozzafava




## ARTICLES

**2,4,6-Trisubstituted pyridines: Synthesis, topoisomerase I and II inhibitory activity, cytotoxicity, and structure–activity relationship** **pp 4351–4359**
Arjun Basnet, Pritam Thapa, Radha Karki, Younghwa Na, Yurngdong Jahng, Byeong-Seon Jeong, Tae Cheon Jeong, Chong-Soon Lee and Eung-Seok Lee*

Designed and synthesized were a series of pyridines substituted at 2, 4, and 6 positions with various 5- or 6-membered heteroaromatics as antitumor agents. They were evaluated for their topoisomerase I and II inhibitory activities along with cytotoxicities against several human cancer cell lines. Among the prepared compounds, **10**–**20** showed significant topoisomerase I or II inhibitory activity, and **21**–**26** showed considerable cytotoxicities against several human cancer cell lines. Structure–activity relationship study indicates that 4′-pyridine at 6-position of central pyridine plays a key role in biological activity.



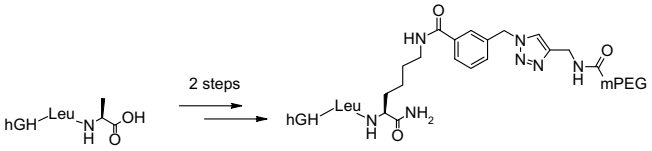

$R^1$, $R^2$ : phenyl
2- or 3-thienyl
2- or 3-furyl
2- or 3- or 4-pyridyl

**Unique O-ribosylation in the biosynthesis of butirosin** **pp 4360–4368**
Fumitaka Kudo, Takuya Fujii, Shunsuke Kinoshita and Tadashi Eguchi*

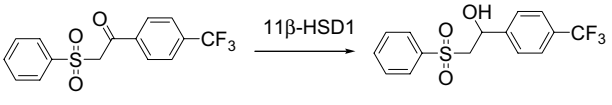
**New antitumoral acetogenin 'Guanacone type' derivatives: Isolation and bioactivity. Molecular dynamics simulation of diacetyl-guanacone** pp 4369–4381
Isabel Barrachina, Inmaculada Royo, Héctor A. Baldoni, Nadia Chahboune, Fernando Suvire, Nuria DePedro, M. Carmen Zafra-Polo, Almudena Bermejo, Noureddine El Aouad, Nuria Cabedo, Jairo Saez, José R. Tormo, Ricardo D. Enriz and Diego Cortes*

We describe herein the isolation and semisynthesis of four acetogenin derivatives (**1**–**4**) as well as their ability to inhibit the mitochondrial respiratory chain and several tumor cell lines. In addition, we have carried out a four nanoseconds (ns) of MD simulation of compound **4**, in a fully hydrated POPC bilayer, as reported.

**C-Terminally PEGylated hGH-derivatives** pp 4382–4395
Bernd Peschke,* Magali Zundel, Sonja Bak, Trine R. Clausen, Niels Blume, Anja Pedersen, Florencio Zaragoza and Kjeld Madsen




**β-Keto sulfones as inhibitors of 11β-hydroxysteroid dehydrogenase type I and the mechanism of action** pp 4396–4405
Jason Xiang,* Manus Ipek, Vipin Suri, May Tam, Yuzhe Xing, Nelson Huang, Yanling Zhang, James Tobin, Tarek S. Mansour and John McKew

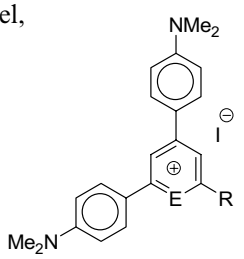



**2a** **7**

**HSD1 $IC_{50}$: 0.187 μM**
**HSD2 $IC_{50}$: 200 μM**

**Synthesis of analogues of a flexible thiopyrylium photosensitizer for purging blood-borne pathogens and binding mode and affinity studies of their complexes with DNA** pp 4406–4418
Ruel E. McKnight,* Mao Ye, Tymish Y. Ohulchanskyy, Sadia Sahabi, Bryan R. Wetzel, Stephen J. Wagner, Andrey Skripchenko and Michael R. Detty*

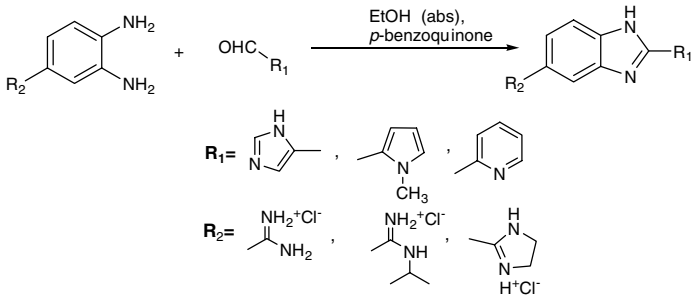
A series of thio- and seleno-analogues of 2,4-di(4-dimethylaminophenyl)-6-methylthiopyrylium iodide was prepared and the binding of these dyes to DNA was examined spectrophotometrically, by isothermal titration calorimetry, by a topoisomerase I assay, by competition dialysis, and by circular dichroism spectroscopy.



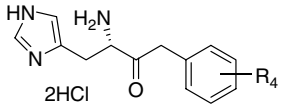

E = S, Se
R = Me, Et, n-Pr, i-Pr, n-Bu, tert-Bu

**Synthesis, antiviral and antitumor activity of 2-substituted-5-amidino-benzimidazoles** **pp 4419–4426**
Kristina Starčević, Marijeta Kralj,* Katja Ester, Ivan Sabol, Magdalena Grce, Krešimir Pavelić and Grace Karminski-Zamola

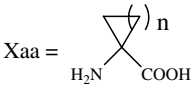
Novel heterocyclic 2-substituted-5-amidino-benzimidazoles were prepared. Compounds having imidazolinylamidine-substituent showed reasonable antiproliferative activity, while all show noticeable selectivity toward breast cancer cells. Strong antiviral activity was obtained by pyridyl-substituted compounds toward coxsackieviruses and echoviruses. Distinct effect toward adenoviruses was also shown.



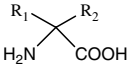

***Brucella suis* histidinol dehydrogenase: Synthesis and inhibition studies of a series of substituted benzylic ketones derived from histidine** **pp 4427–4433**
Marie-Rose Abdo, Pascale Joseph, Rose-Anne Boigegrain, Jean-Pierre Liautard, Jean-Louis Montero, Stephan Köhler* and Jean-Yves Winum*




**Synthesis and biological activity of nociceptin/orphanin FQ analogues substituted in position 7 or 11 with Cα,α-dialkylated amino acids** **pp 4434–4443**
Marika Arduin, Barbara Spagnolo, Girolamo Calò, Remo Guerrini,* Giacomo Carrà, Carmela Fischetti, Claudio Trapella, Erika Marzola, John McDonald, David G. Lambert, Domenico Regoli and Severo Salvadori



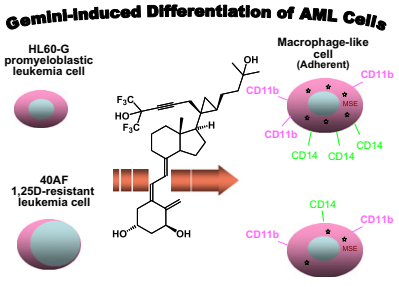

Ac$_X$c: n = 1, 3, 4



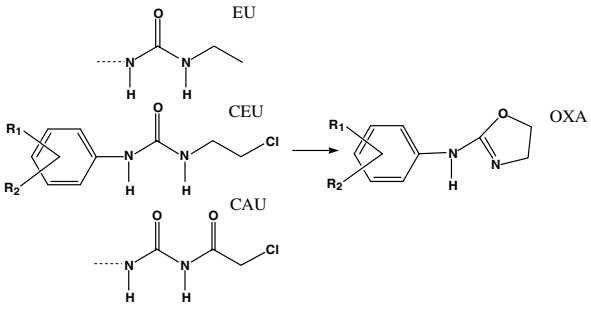

Aib: R1=Me, R2=Me; Iva: R1=Me, R2=Et;
Deg: R1=Et, R2=Et; Dpg: R1=nPr, R2=nPr;
(αMe)Val: R1=Me, R2=iPr;
(αMe)Leu: R1=Me, R2=iBu

Two series of compounds substituted in position 7 or 11 with Cα,α-disubstituted amino acids were synthesised and pharmacologically evaluated; new potent NOP receptor agonists were identified.

**Calcitriol derivatives with two different side-chains at C-20. Part 4: Further chain modifications that alter VDR-dependent monocytic differentiation potency in human leukemia cells** **pp 4444–4455**
Edward Garay, Pawel Jankowski, Paulo Lizano, Stanislaw Marczak, Hubert Maehr, Luciano Adorini, Milan R. Uskokovic and George P. Studzinski*



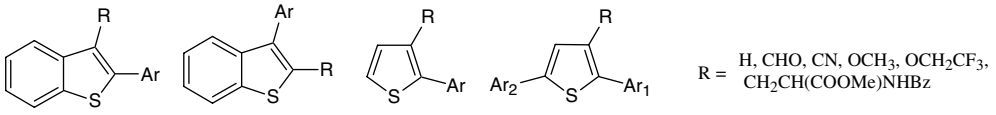
**Alkylation potency and protein specificity of aromatic urea derivatives and bioisosteres as potential irreversible antagonists of the colchicine-binding site** **pp 4456–4469**
Jessica S. Fortin,* Jacques Lacroix, Michel Desjardins, Alexandre Patenaude, Éric Petitclerc and René C.-Gaudreault*




**3D-QSAR studies on malonyl coenzyme A decarboxylase inhibitors** **pp 4470–4481**
Maulik R. Patel and Tanaji T. Talele*

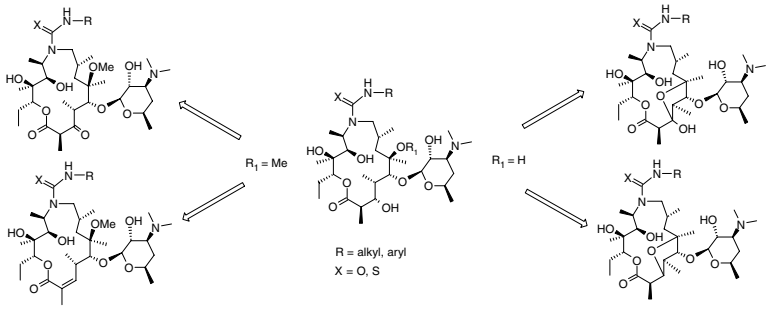
3D-QSAR study using CoMFA and CoMSIA methods was carried out on a diverse set of malonyl coenzyme A decarboxylase (MCD) inhibitors. The CoMFA and CoMSIA models showed excellent predictive capabilities.

**Synthesis and evaluation of new arylbenzo[*b*]thiophene and diarylthiophene derivatives as inhibitors of the NorA multidrug transporter of *Staphylococcus aureus*** **pp 4482–4497**
Jérémie Fournier dit Chabert, Béatrice Marquez, Luc Neville, Lionel Joucla, Sylvie Broussous, Pascale Bouhours, Emilie David, Stéphane Pellet-Rostaing,* Bernard Marquet, Nicole Moreau and Marc Lemaire

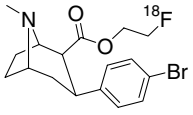



New arylbenzo[*b*]thiophene and arylthiophene derivatives were synthesised and evaluated as inhibitors of the NorA multidrug transporter of *Staphylococcus aureus*.

**Novel 9a-carbamoyl- and 9a-thiocarbamoyl-3-decladinosyl-6-hydroxy and 6-methoxy derivatives of 15-membered macrolides** **pp 4498–4510**
Zorica Marušić Ištuk, Stjepan Mutak, Nedjeljko Kujundžić and Goran Kragol*



**Synthesis and radiopharmacological characterization of 2β-carbo-2′-[$^{18}$F]fluoroethoxy-3β-(4-bromophenyl)tropane ([$^{18}$F]MCL-322) as a PET radiotracer for imaging the dopamine transporter (DAT)** pp 4511–4519
F. Wuest,* M. Berndt, K. Strobel, J. van den Hoff, X. Peng, J. L. Neumeyer and R. Bergmann

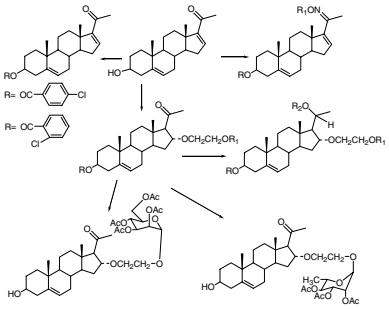



[$^{18}$F]MCL-322

The simple single-step radiosynthesis and radiopharmacological characterization of [$^{18}$F]MCL-322 as novel radiotracer for imaging DAT is described.

**Expeditious and convenient synthesis of pregnanes and its glycosides as potential anti-dyslipidemic and anti-oxidant agents** pp 4520–4527
Arun Sethi,* Atul Maurya, Vibha Tewari, Sanjay Srivastava, Shaheen Faridi, Gitika Bhatia, M. M. Khan, A. K. Khanna and J. K. Saxena

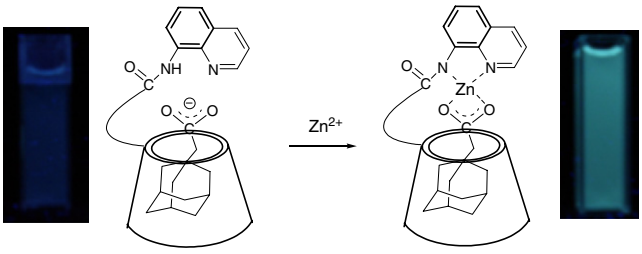
Expeditious and convenient procedures for the synthesis of newer pregnane derivatives and its glycosides are reported. Amongst them compound **3** and **7** showed more lipid lowering and anti-oxidant activity as compared to other compounds.



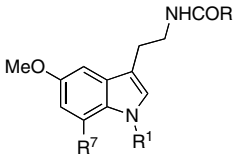
**Novel acyclic enediynes inhibit Cyclin A and Cdc25C expression and induce apoptosis phenomenon to show potent antitumor proliferation** pp 4528–4536
Yu-Hsiang Lo, I-Ling Lin, Chi-Fong Lin, Cheng-Chung Hsu, Sheng-Huei Yang, Shinne-Ren Lin and Ming-Jung Wu*

Enediynes showed most potent growth inhibition activity against all tumor cell lines in low concentration and almost completely blocked cell cycle in G2/M phase via controlling Cyclin A and Cdc25C expression and apoptosis.

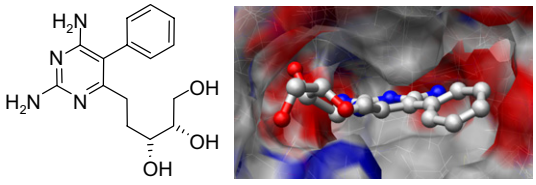
**Effective switch-on fluorescence sensing of zinc(II) ion by 8-aminoquinolino-β-cyclodextrin/adamantaneacetic acid system in water** pp 4537–4542
Yong Chen, Kun-Ying Han and Yu Liu*



**7-Substituted-melatonin and 7-substituted-1-methylmelatonin analogues: Effect of substituents on potency and binding affinity** pp 4543–4551
Rüdiger Faust, Peter J. Garratt, Maria Angeles Trujillo Pérez, Vincent J.-D. Piccio, Christian Madsen, Ane Stenstrøm, Bente Frølund, Kathryn Davidson, Muy-Teck Teh and David Sugden*

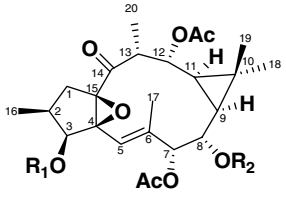



**Structure-based design, synthesis and preliminary evaluation of selective inhibitors of dihydrofolate reductase from *Mycobacterium tuberculosis*** pp 4552–4576
Mervat H. R. I. El-Hamamsy, Anthony W. Smith, Andrew S. Thompson and Michael D. Threadgill*




Linking a glycerol-mimicking triol to a pyrimidine-2,4-diamine gives a molecule which occupies both the dihydrofolate- and glycerol-binding pockets of *Mycobacterium tuberculosis* DHFR, leading to species-selective inhibition.

**Isolation of new phenylacetylingol derivatives that reactivate HIV-1 latency and a novel spirotriterpenoid from *Euphorbia officinarum* latex** pp 4577–4584
Mourad Daoubi, Nieves Marquez, Noureddine Mazoir, Ahmed Benharref, Rosario Hernández-Galán, Eduardo Muñoz and Isidro G. Collado*




The biological effects of new ingol diterpenes (**1**–**3**) on cell cycle and HIV-1 gene transcription were analysed. Compound **3** induced cell-cycle arrest and HIV-1-LTR promoter activation.

**Explaining cyclodextrin–mycotoxin interactions using a 'natural' force field** pp 4585–4594
Alessio Amadasi, Chiara Dall'Asta, Gianluigi Ingletto, Roberto Pela, Rosangela Marchelli and Pietro Cozzini*

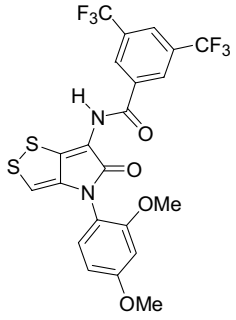
Predicted inclusion mechanism of ochratoxin A into β-cyclodextrin. The Connolly surface of the host (cyclodextrin), built using Sybyl MOLCAD tools, is coloured blue, while the guest molecule (ochratoxin A) is rendered in capped sticks.

**Binding of ring-substituted indole-3-acetic acids to human serum albumin** **pp 4595–4600**
Milan Šoškić* and Volker Magnus

A quantitative model is proposed which accurately predicts the binding affinities of ring-substituted indole-3-acetic acids to human serum albumin.

**Substituted 6-amino-4*H*-[1,2]dithiolo[4,3-*b*]pyrrol-5-ones: Synthesis, structure–activity relationships, and cytotoxic activity on selected human cancer cell lines** **pp 4601–4608**
Bin Li,* Michael P. A. Lyle,* Genhui Chen, Jason Li, Kaiji Hu, Liren Tang, Moulay A. Alaoui-Jamali and John Webster

This paper describes the efficient synthesis and anti-cancer activity of a series of substituted 6-amino-4*H*-[1,2]dithiolo[4,3,-*b*]pyrrol-5-ones.



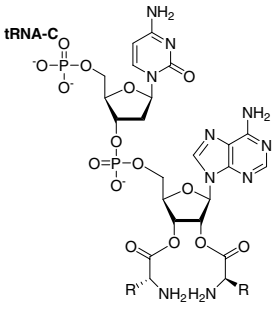

**2D QSAR studies on thyroid hormone receptor ligands** **pp 4609–4617**
Napoleão F. Valadares,* Marcelo S. Castilho, Igor Polikarpov and Richard C. Garratt

In our studies SYBYL 7.2 was used to obtain predictive HQSAR models for TRα ($q^2$ = 0.78) and TRβ ($q^2$ = 0.69) which proved more valuable than the classical 2D-QSAR. Contribution map analysis identified a number of positions that could be useful to the development of receptor isoform specific ligands.

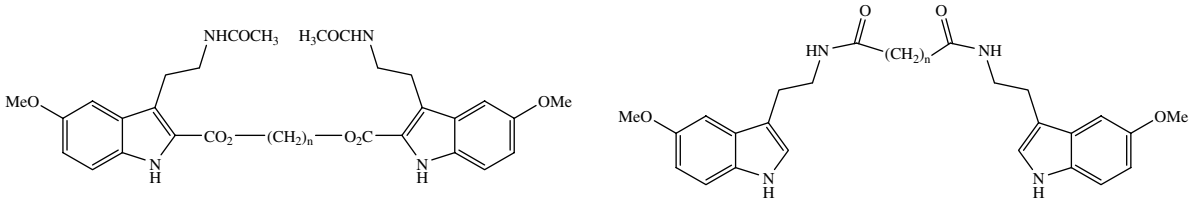
**Resisting degradation by human elastase: Commonality of design features shared by 'canonical' plant and bacterial macrocyclic protease inhibitor scaffolds** **pp 4618–4628**
Arnd B. E. Brauer,* Jeffrey D. McBride, Geoff Kelly, Stephen J. Matthews and Robin J. Leatherbarrow*

**Synthesis of bisaminoacylated pdCpAs and tandemly activated transfer RNAs** **pp 4629–4642**
Maria Duca, David J. Maloney, Michiel Lodder, Bixun Wang and Sidney M. Hecht*

Bisaminoacylated tRNAs, at least one of which has been reported to occur naturally in a thermophilic bacterium, have been shown to function in in vitro protein synthesis. The preparation of several bisaminoacylated pdCpAs and their conversion to bisaminoacyl-tRNAs is described.




**Synthesis and biological activity of new melatonin dimeric derivatives** **pp 4643–4650**
Barbara Di Giacomo,* Annalida Bedini, Gilberto Spadoni, Giorgio Tarzia, Franco Fraschini, Marilou Pannacci and Valeria Lucini




**Zinc-(II) 2,9,16,23-tetrakis (methoxy) phthalocyanine: Potential photosensitizer for use in photodynamic therapy in vitro** **pp 4651–4660**
Edith I. Yslas, Edgardo N. Durantini and Viviana A. Rivarola*

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**Summary of instructions to authors** **p I**

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

## COVER

Commonality of bacterial (left) and plant-derived (right) serine protease inhibitor scaffolds as described by Brauer *et al.* with a particular highlight on the interaction of the conserved P2 threonine with the enzyme's catalytic triad (cyan); the images were generated by Daniel Baum (ZIB) with AmiraMol based on PDB coordinates 1OKX and 1HD9 [Brauer, A. B. E.; McBride, J. D.; Kelly, G.; Matthews, S. J.; Leatherbarrow, R. J. *Bioorg. Med. Chem.* **2007**, *15,* 4618–4628].

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