

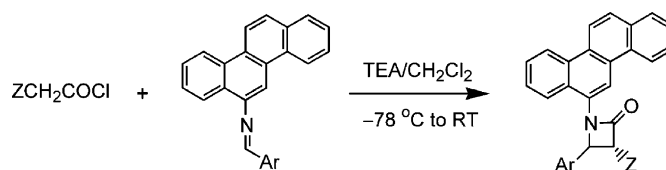
## Contents

### ARTICLES

#### Stereocontrolled synthesis of anticancer $\beta$ -lactams via the Staudinger reaction

pp 3611–3622

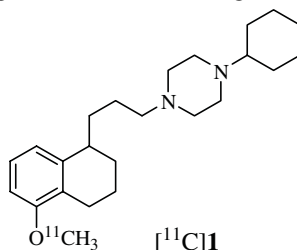
Bimal K. Banik,\* Indrani Banik and Frederick F. Becker



#### Synthesis and in vivo evaluation of a new PET radioligand for studying sigma-2 receptors

pp 3623–3626

Michael Kassiou,\* Robert F. Dannals, Xiang Liu, Dean F. Wong, Hayden T. Ravert and Ursula A. Scheffel

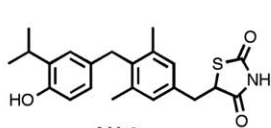


1-Cyclohexyl-4-[3-(5-methoxy-1,2,3,4-tetrahydro-naphthalen-1-yl)-propyl]-piperazine **1** is a high affinity sigma-2 ligand, which has been labelled with carbon-11 ( $t_{1/2}$ : 20.4 min) and evaluated in vivo in the mouse brain as a potential positron-emission-tomography (PET) radioligand.

#### Design and synthesis of complementing ligands for mutant thyroid hormone receptor TR $\beta$ (R320H): a tailor-made approach toward the treatment of resistance to thyroid hormone

pp 3627–3639

Atsushi Hashimoto, Youheng Shi, Katherine Drake and John T. Koh\*

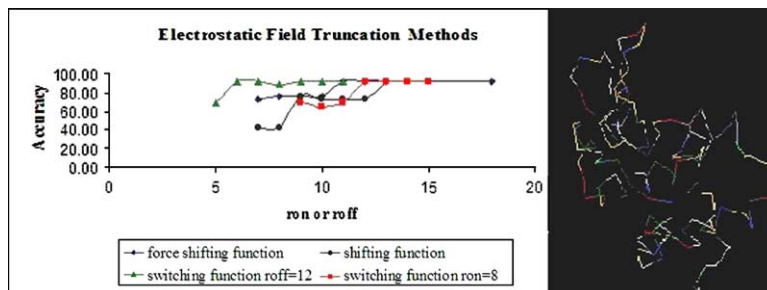
	EC <sub>50</sub> (nM)/ (efficacy, %max)				
	TRa	TRb	RTH-associated mutants		
			R320H	R320C	R316H
			equal	equal	-196 fold
	0.47 ± 0.13 (100)	0.54 ± 0.07 (100)	0.46 ± 0.05 (120)	0.67 ± 0.15 (120)	105.8 ± 16.5 (110)
AH-9					



### Proteins Markovian 3D-QSAR with spherically-truncated average electrostatic potentials

pp 3641–3647

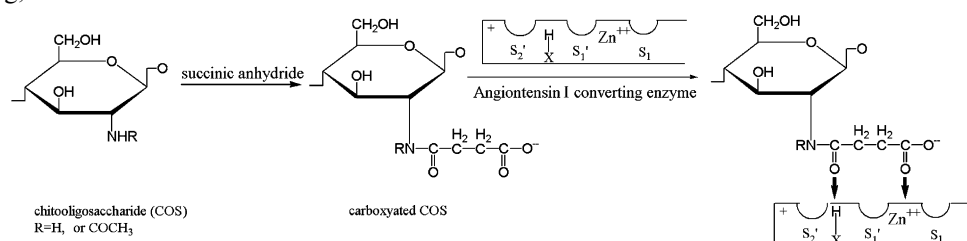
Liane Saíz-Urra, Humberto González-Díaz\* and Eugenio Uriarte



### Improvement of ACE inhibitory activity of chitoooligosaccharides (COS) by carboxyl modification

pp 3649–3655

Ronghua Huang, Eresha Mendis and Se-Kwon Kim\*

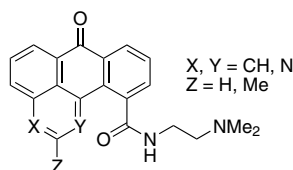


COCH<sub>2</sub>CH<sub>2</sub>COO<sup>-</sup> group, which is similar to Captopril<sup>®</sup> in structure, was introduced to chitoooligosaccharides (COS). Angiotensin I converting enzyme (ACE) inhibitory activity of COS was successfully improved by the introduced group. ACE inhibitory mechanism of COS derivative was competitive via obligatory binding site of the enzyme.

### Synthesis and cytotoxic activity of *N*-[(alkylamino)alkyl]carboxamide derivatives of 7-oxo-7*H*-benz[*de*]anthracene, 7-oxo-7*H*-naphtho[1,2,3-*de*]quinoline, and 7-oxo-7*H*-benzo[*e*]perimidine

pp 3657–3665

Xianyong Bu, Junjie Chen, Leslie W. Deady,\* Clare L. Smith, Bruce C. Baguley, Debra Greenhalgh, Shangjin Yang and William A. Denny\*

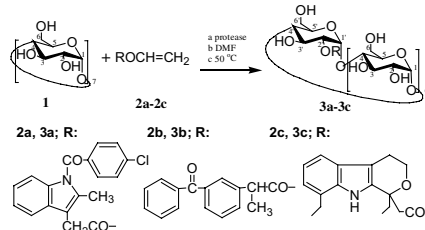


We discuss the synthesis and structure–cytotoxicity relationships of GC-selective naphthoquinoline-11-carboxamides and analogues. Examples showed high activity in the mouse colon 38 tumor model.

### Regioselective synthesis of cyclodextrin mono-substituted conjugates of non-steroidal anti-inflammatory drugs at C-2 secondary hydroxyl by protease in non-aqueous media

pp 3667–3671

Na Wang, Qi Wu, Yong Mei Xiao, Chun Xiu Chen and Xian Fu Lin\*



Three 2-*O*-mono-substituted β-cyclodextrin (β-CD) conjugates of indomethacin, ketoprofen and etodolac were synthesized by enzymatic methods.

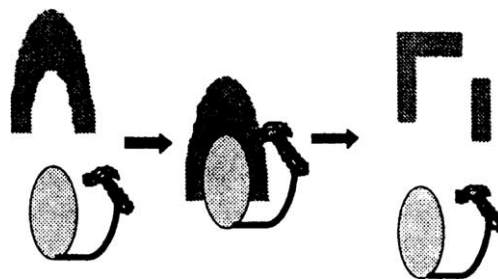


**An artificial aspartic proteinase system**

pp 3673–3680

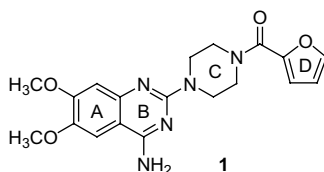
Lin Jiang, Zhilian Liu, Zhi Liang and Yunhua Gao\*

A series of crown ether compounds can selectively complex some specific esters and the carboxyls in their molecules play the role of a hammer just as depicted in the graphic to cleave ester bonds by nucleophilic catalysis, which partially simulates some aspartic proteinases in the case of catalytic mechanisms.

**Search for the pharmacophore in prazosin for Transport-P**

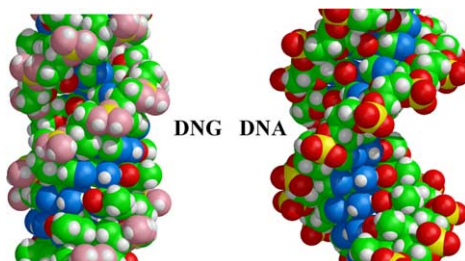
pp 3681–3689

Patricia A. Zunszain, Cesare Federico, Mario Sechi, Saad Al-Damluji and C. Robin Ganellin\*

**Comparison of positively charged DNG with DNA duplexes: a computational approach**

pp 3691–3698

Joseph W. Toporowski, Swarnalatha Y. Reddy and Thomas C. Bruice\*

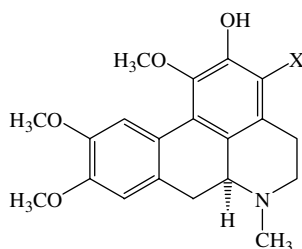


Molecular dynamics is used to investigate the structural properties of the cationic DNA analogue deoxynucleic guanidine (DNG), in which a guanidinium group replaces the phosphate moiety of DNA.

**Structure–affinity relationships of halogenated prednicentrine and glaucine derivatives at D<sub>1</sub> and D<sub>2</sub> dopaminergic receptors: halogenation and D<sub>1</sub> receptor selectivity**

pp 3699–3704

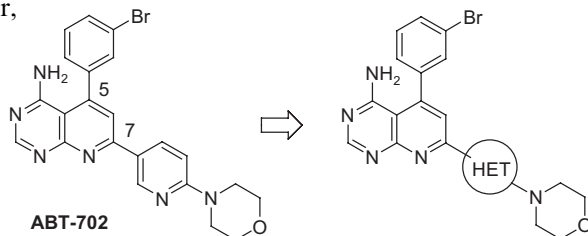
Marcelo Asencio, Claudio Hurtado-Guzmán, John J. López, Bruce K. Cassels,\*  
Philippe Protais and Abdeslam Chagraoui



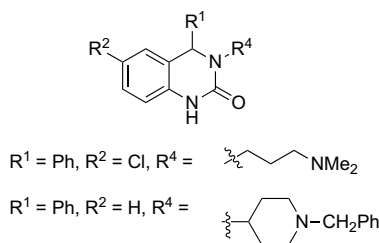
2-Hydroxyaporphines bearing a halogen atom at C-3 are potent, selective D<sub>1</sub> dopaminergic ligands.

**5-(3-Bromophenyl)-7-(6-morpholin-4-ylpyridin-3-yl)pyrido[2,3-*d*]pyrimidin-4-ylamine: structure–activity relationships of 7-substituted heteroaryl analogs as non-nucleoside adenosine kinase inhibitors** pp 3705–3720

Mark A. Matulenko,\* Chih-Hung Lee, Meiqun Jiang, Robin R. Frey, Marlon D. Cowart, Erol K. Bayburt, Stanley DiDomenico, Gregory A. Gfesser, Arthur Gomtsyan, Guo Zhu Zheng, Jeffery A. McKie, Andrew O. Stewart, Haixia Yu, Kathy L. Kohlhaas, Karen M. Alexander, Steve McGaraughty, Carol T. Wismer, Joseph Mikusa, Kennan C. Marsh, Ronald D. Snyder, Marilyn S. Diehl, Elizabeth A. Kowaluk, Michael F. Jarvis and Shripad S. Bhagwat


**A novel class of sodium/calcium exchanger inhibitor: design, synthesis, and structure–activity relationships of 3,4-dihydro-2(1*H*)-quinazolinone derivatives** pp 3721–3735

Hirohiko Hasegawa,\* Masami Muraoka, Mikiko Ohmori, Kazuki Matsui and Atsuyuki Kojima


**The role of hydrophobic properties of chemicals in promoting allosteric reactions** pp 3737–3762

Suresh B. Mekapati, Alka Kurup, Rajeshwar P. Verma and Corwin Hansch\*

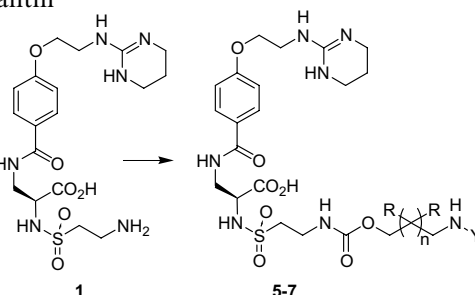
The QSAR model for the role of hydrophobic properties of chemicals in promoting allosteric reactions may be illustrated by Eq. I.

$$\log 1/C = -a \log P + b \log P^2 \pm \text{constant} \quad (\text{I})$$

**Synthesis, in vitro, and in vivo characterization of an integrin  $\alpha_v\beta_3$ -targeted molecular probe for optical imaging of tumor** pp 3763–3771

Christopher A. Burnett, Jianwu Xie, Jade Quijano, Zhimin Shen, Finie Hunter, Monica Bur, King C. P. Li and S. Narasimhan Danthi\*

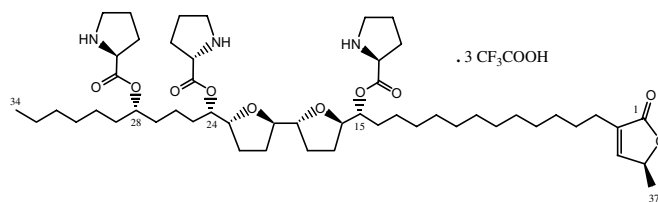
Integrin-targeted optical probe **7** was synthesized by coupling **6a** to fluorescein isothiocyanate and the in vitro and in vivo characterization of the probe was studied. In addition, several carbamate derivatives of compound **1** were synthesized in order to investigate the structure–activity relationship potential beyond its amine terminus. All synthesized derivatives of **1** demonstrated equal or increased binding affinity for integrin  $\alpha_v\beta_3$ .



Cmpd	n	R	Y
<b>5a</b>	1	CH <sub>3</sub>	Boc
<b>5b</b>	0	H	Boc
<b>5c</b>	1	H	Boc
<b>5d</b>	2	H	Boc
<b>6a</b>	1	CH <sub>3</sub>	H
<b>6b</b>	0	H	H
<b>6c</b>	1	H	H
<b>6d</b>	2	H	H
<b>7</b>	1	CH <sub>3</sub>	Fluorescein

**Semisynthesis and biological activity of aminoacyl triesters of squamocin, an annonaceous acetogenin** pp 3773–3781

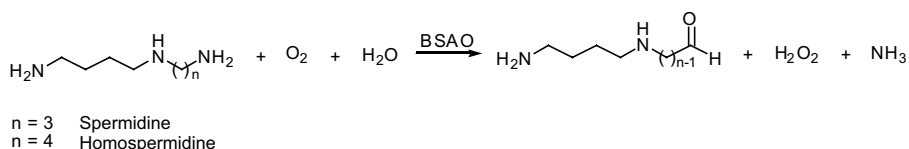
Romain A. Duval, Philippe Duret, Guy Lewin,\* Eva Peris and Reynald Hocquemiller



Aminoacyl triesters of squamocin have been synthesized in two to three steps from protected (L)-aminoacids and squamocin, and evaluated for their inhibitory activity of mitochondrial complex I and cytotoxicity against KB 3-1 cells in vitro. All triesters derivatives exhibited an extinction of activity at the enzymatic level, correlated to a reduced though modulated cytotoxicity relatively to squamocin.

**Substrate specificity of the bovine serum amine oxidase and in situ characterisation of aminoaldehydes by NMR spectroscopy** pp 3783–3796

Gunnar Houen,\* Casper Struve, Roar Søndergaard, Tina Friis, Uffe Anthoni, Per H. Nielsen, Carsten Christophersen, Bent O. Petersen and Jens Ø. Duus

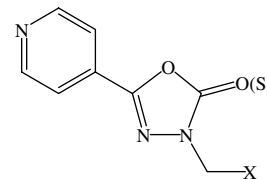


The bovine serum amine oxidase (BSAO)-catalysed oxidation of spermidine and homospermidine has been monitored by  $^1\text{H}$  NMR spectroscopy in water with 10%  $\text{D}_2\text{O}$ .

**Antimycobacterial activity of new 3-substituted 5-(pyridin-4-yl)-3H-1,3,4-oxadiazol-2-one and 2-thione** pp 3797–3809

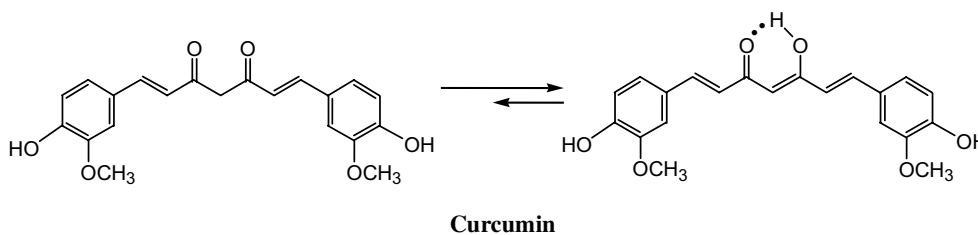
Maria Grazia Mamolo,\* Daniele Zampieri, Luciano Vio, Maurizio Fermeglia, Marco Ferrone, Sabrina Pricl, Giuditta Scialino and Elena Banfi

3H-1,3,4-Oxadiazole-2-thione and 3H-1,3,4-oxadiazol-2-one derivatives were synthesized and tested for their in vitro antimycobacterial activity. Oxadiazolone derivatives showed an interesting antimycobacterial activity against the tested strain of *Mycobacterium tuberculosis* H<sub>37</sub>Rv, whereas the corresponding thione derivatives were devoid of activity. Molecular modeling investigations showed that the active compounds may interact at the active site of the mycobacterial cytochrome P450-dependent sterol 14 $\alpha$ -demethylase in the sterol biosynthesis pathway and that their binding free energy values are in agreement with their MIC values.

**Anti-oxidant activities of curcumin and related enones**

pp 3811–3820

Waylon M. Weber, Lucy A. Hunsaker, Steve F. Abcouwer, Lorraine M. Deck\* and David L. Vander Jagt\*

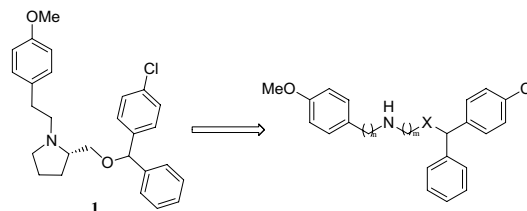


### Investigation into the structure–activity relationship of novel concentration dependent, dual action T-type calcium channel agonists/antagonists

pp 3821–3839

William F. McCalmont,\* Jaclyn R. Patterson, Michael A. Lindenmuth, Tiffany N. Heady, Doris M. Haverstick, Lloyd S. Gray and Timothy L. Macdonald

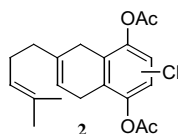
This paper describes the synthesis and biological evaluation of a library of compounds that are based on the structure of compound **1**, which has been shown to be a T-type calcium channel antagonist, as well as exhibits anti-proliferative activity against a variety of tumor cell lines. These new analogs of compound **1** not only show better antagonist activity toward calcium influx and anti-proliferation, at higher concentrations they also show an agonist activity toward calcium influx.



### Synthesis, characterisation and cytotoxicity of chloro derivatives of prenylnaphthohydroquinone

pp 3841–3846

Aurora Molinari,\* Alfonso Oliva, Claudia Ojeda, Jorge Escobar, Carolina Gallardo, José M<sup>a</sup> Miguel del Corral, M<sup>a</sup> Angeles Castro, Carmen Cuevas and Arturo San Feliciano

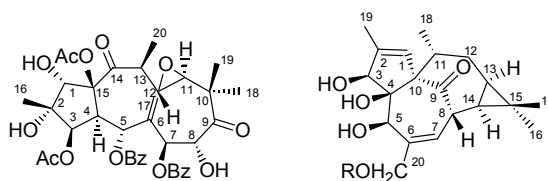


A family of chloroprenylnaphthohydroquinone derivatives have been synthesised from the acetylated Diels–Alder product **2**, of  $\alpha$ -myrcene and 2-chloro-1,4-benzoquinone. This family has been evaluated for their cytotoxicity against several neoplastic cell lines.

### Mechanism of proliferation arrest of embryonic cells of *Xenopus* by diterpene compounds

pp 3847–3851

Tomoharu Okouchi, Tetsuya Abe, Shusuke Araki, Shinsuke Arai, Takashi Iida, Li-Yan Wang, Susumu Kitanaka and Shohei Miyata\*

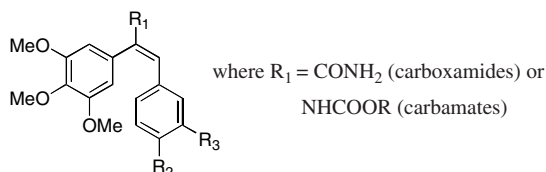


Kansuinin and ingenol compounds arrest cell proliferation by inhibition of reactions in specific cell cycle.

### New antitubulin derivatives in the combretastatin A4 series: synthesis and biological evaluation

pp 3853–3864

Christine Borrel, Sylviane Thoret, Xavier Cachet, Daniel Guénard, François Tillequin, Michel Koch and Sylvie Michel\*




A series of carboxamide and carbamate analogues of combretastatin A4 were synthesized and evaluated. Several compounds exhibited strong cytotoxicities correlated with a potent inhibition of tubulin assembling.

**OTHER CONTENTS**

Contributors to this issue  
Instructions to contributors

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\*Corresponding author

 Supplementary data available via ScienceDirect

**COVER**

2005: Human liver glycogen phosphorylase A (HLGPa) is an attractive target enzyme for discovering anti-type 2 diabetes drugs. This picture shows the interaction model for a series of indole-2-carboxamides to HLGPa derived from molecular docking simulations [Liu, G.; Zhang, Z.; Luo, X.; Shen, J.; Liu, H.; Shen, X.; Chen, K.; Jiang, H. *Bioorg. Med. Chem.* **2004**, *12*, 4147–4157].



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