

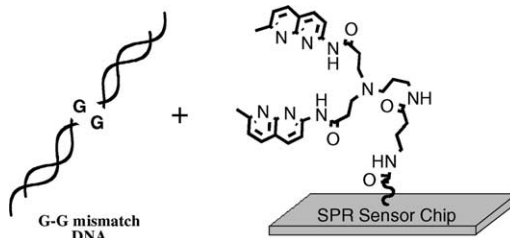
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### ARTICLES

**The binding of guanine–guanine mismatched DNA to naphthyridine dimer immobilized sensor surfaces: kinetic aspects**

pp 3117–3123

Kazuhiko Nakatani,\* Akio Kobori, Hiroyuki Kumasawa, Yuki Goto and Isao Saito

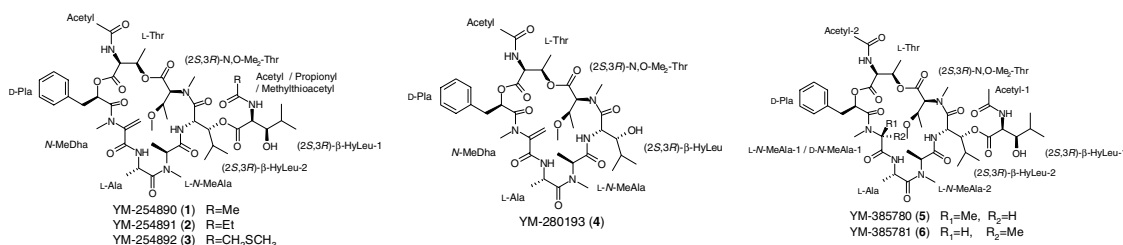


The kinetics for the binding of the G–G mismatch to the naphthyridine dimer was investigated by surface plasmon resonance assay.

**YM-254890 analogues, novel cyclic depsipeptides with  $\alpha_q/11$  inhibitory activity from *Chromobacterium* sp. QS3666**

pp 3125–3133

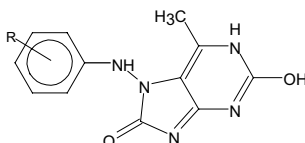
Masatoshi Taniguchi,\* Ken-ichi Suzumura, Koji Nagai, Tomihisa Kawasaki, Jun Takasaki, Mitsuhiro Sekiguchi, Yumiko Moritani, Tetsu Saito, Kazumi Hayashi, Shigeo Fujita, Shin-ichi Tsukamoto and Ken-ichi Suzuki



**Synthesis and in vitro antimicrobial activities of 2-hydroxy-6-methyl-7-(arylamino)-1,7-dihydropurin-8-ones**

pp 3135–3139

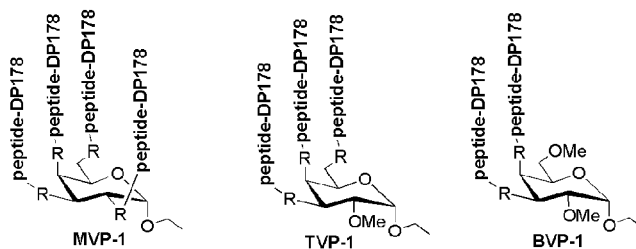
Pratibha Sharma,\* Shikha Sharma and Nilesh Rane



A series of 2-hydroxy-6-methyl-7-(arylamino)-1,7-dihydropurin-8-ones have been synthesized. Their chemical structures were confirmed by spectral and elemental analysis data. These synthesized compounds were subjected to antibacterial activity against Gram-positive and Gram-negative bacteria using a reference antibiotic drug purinthol as control. Molecular refractive index parameters ( $M_R$ ) and Hammett substituent constant ( $\sigma$ ) have also been calculated to study quantitative structure–activity relationship.

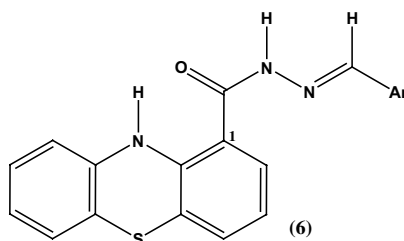
**Synthesis, conformation, and immunogenicity of monosaccharide-centered multivalent HIV-1 gp41 peptides containing the sequence of DP178** pp 3141–3148

Jiahong Ni, Robert Powell, Ilia V. Baskakov, Anthony DeVico, George K. Lewis and Lai-Xi Wang\*



**New class of potent antinociceptive and antiplatelet 10*H*-phenothiazine-1-acylhydrazone derivatives** pp 3149–3158

Gildásio A. Silva, Luciana M. M. Costa, Fernanda C. F. Brito, Ana L. P. Miranda, Eliezer J. Barreiro and Carlos A. M. Fraga\*



The synthesis and pharmacological evaluation of new 10*H*-phenothiazine-1-acylhydrazone derivatives (6) is reported.

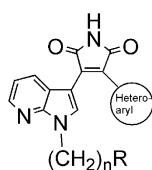
**A novel 3D-QSAR comparative molecular field analysis (CoMFA) model of imidazole and quinazolinone functionalized p38 MAP kinase inhibitors** pp 3159–3166

Gilberto M. Sperandio da Silva, Carlos M. R. Sant'Anna and Eliezer J. Barreiro\*

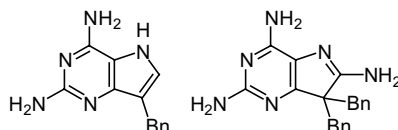
A new CoMFA model of dihydroquinazolinone and tetrasubstituted imidazole compounds with p38 MAPK inhibitory activity is reported.

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David J. O'Neill, Lan Shen, Catherine Prouty, Bruce R. Conway, Lori Westover, Jun Z. Xu, Han-Cheng Zhang, Bruce E. Maryanoff, William V. Murray, Keith T. Demarest and Gee-Hong Kuo\*

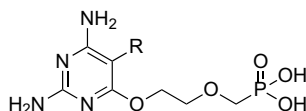


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**Synthesis and antiviral activity of 2,4-diamino-5-cyano-6-[2-(phosphonomethoxy)ethoxy]pyrimidine and related compounds** pp 3197–3202

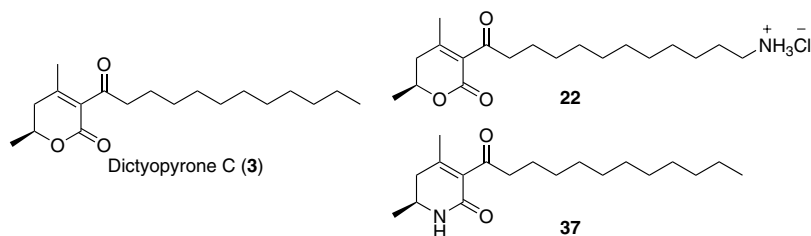
Dana Hocková,\* Antonín Holý, Milena Masojídková, Graciela Andrei, Robert Snoeck, Erik De Clercq and Jan Balzarini



R = CN, CHO

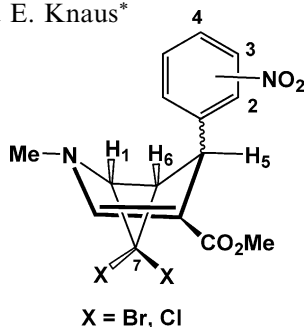
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Haruhisa Kikuchi, Kazunori Sasaki, Jun'ichi Sekiya, Yasuo Maeda, Aiko Amagai, Yuzuru Kubohara and Yoshiteru Oshima\*



**Design and synthesis of methyl 2-methyl-7,7-dihalo-5-phenyl-2-azabicyclo[4.1.0]hept-3-ene-4-carboxylates with calcium channel antagonist activity** pp 3215–3220

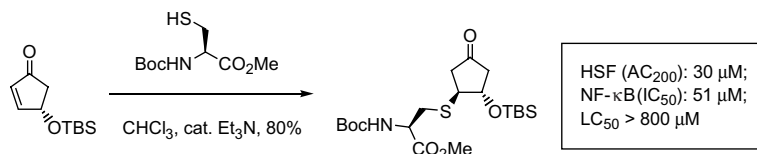
Javid S. Mojarad, Ramin Miri and Edward E. Knaus\*



**Reactions of some cyclopentenones with selected cysteine derivatives and biological activities of the product thioethers**

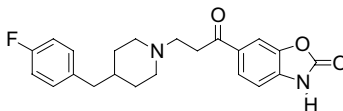
pp 3221–3227

Jamie F. Bickley, Alessandra Ciucci, Paul Evans,\* Stanley M. Roberts, Nicolette Ross and M. Gabriella Santoro


**Radiosynthesis and pharmacological evaluation of [<sup>11</sup>C]EMD-95885: a high affinity ligand for NR2B-containing NMDA receptors**

pp 3229–3237

G. Roger, F. Dollé, B. de Bruin, X. Liu, L. Besret, Y. Bramoullé, C. Coulon, M. Ottaviani, M. Bottlaender, H. Valette and M. Kassiou\*

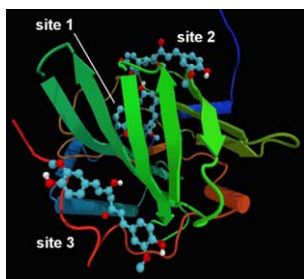


EMD-95885, 6-[3-[4-(4-fluorobenzyl)piperidino]propionyl]-3*H*-benzoxazol-2-one (**1**), a selective NR2B subtype antagonist, has been labelled with carbon-11 (*T*<sub>1/2</sub>: 20.4 min) and in vivo pharmacologically evaluated as a potential positron emission tomography (PET) radioligand for imaging the NMDA receptor.

**Induced circular dichroism spectra reveal binding of the antiinflammatory curcumin to human α<sub>1</sub>-acid glycoprotein**

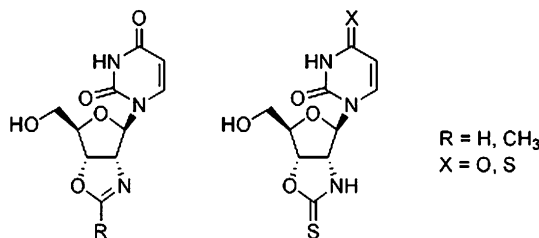
pp 3239–3245

Ferenc Zsila,\* Zsolt Bikádi and Miklós Simonyi


**Novel bicyclic sugar modified nucleosides: synthesis, conformational analysis and antiviral evaluation**

pp 3247–3257

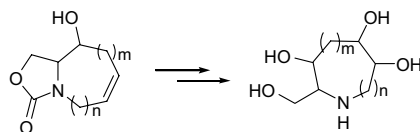
Nurolaini Kifli, Thet Thet Htar, Erik De Clercq, Jan Balzarini and Claire Simons\*



Two novel conformationally restrained alkyl derivatives of 2',3'-dideoxy-2',3'-oxazole-β-D-uridine and a novel uridine 2',3'-thio-carbamate were prepared and conformational parameters determined using MACROMODEL V.6.0 molecular modelling programme. The novel nucleosides were evaluated against a wide range of viral types and strains in cell culture.

### Versatile approach for the synthesis of novel seven-membered iminocyclitols via ring-closing metathesis dihydroxylation reaction

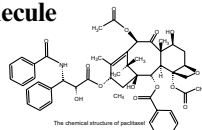
Chang-Ching Lin, Yi-shin Pan, Laxmikant N. Patkar, Hsiu-Mei Lin, Der-Lii M. Tzou, Thangaiah Subramanian and Chun-Cheng Lin\*



### Paclitaxel–HSA interaction. Binding sites on HSA molecule

pp 3269–3275

Lilianna Trynda-Lemiesz\*

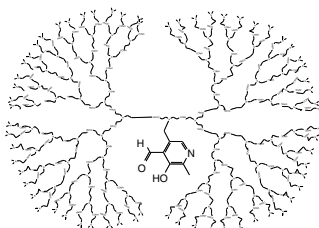


It is used to treat several cancers including tumours of the breast, ovary and lung. The effect of paclitaxel on rapidly dividing cancer cells is based on the ability to bind and stabilize microtubules, thus leading to the block of cell replication in the late  $G_2$ –M phase of the cell cycle. In the present work the interaction of paclitaxel with human serum albumin (HSA) in aqueous solution at physiological pH has been investigated through CD, fluorescence spectroscopy and by the antibody precipitate test. Binding of paclitaxel to albumin impact on protein structure and it influences considerably albumin binding of other molecules like warfarin, heme or bilirubin. The paclitaxel–HSA interaction causes the conformational changes with the loss of helical stability of protein and local perturbation in the domain IIA binding pocket. The relative fluorescence intensity of the paclitaxel-bound HSA decreased, suggesting that perturbation around the Trp 214 residue took place. This was confirmed by the destabilization of the warfarin binding site located in subdomain IIA. CD and fluorescence spectroscopic results showed marked reductions (about 50% decrease in the CD Cotton effect intensity, and ~35% decrease of the fluorescence intensity) in the affinity of albumin for bilirubin upon paclitaxel binding. These results suggested that paclitaxel molecule is bound in the vicinity of Trp 214, which forms part of the wall in one of the two main drug-binding cavities of HSA (site I subdomain IIA).

### Polymeric and dendrimeric pyridoxal enzyme mimics

pp 3277–3287

Lei Liu and Ronald Breslow\*



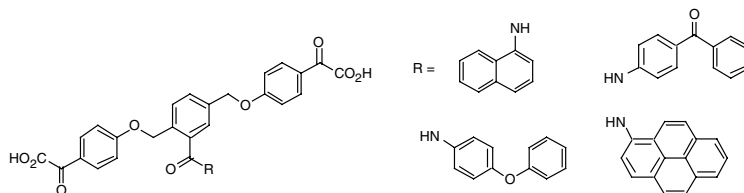
Pyridoxal was covalently attached to polyethylenimine polymers, but the resulting materials were found to degrade rapidly. In comparison, G1 to G6 poly(amide amine) dendrimers with a pyridoxal core were synthesized and these compounds are relatively stable. Their reactivities in catalyzing racemization and decarboxylation reactions of  $\alpha$ -amino acids were studied.



### Parallel synthesis of a library of bidentate protein tyrosine phosphatase inhibitors based on the $\alpha$ -ketoacid motif

pp 3289–3298

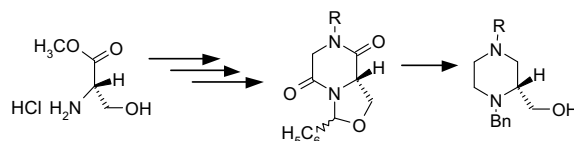
Yen Ting Chen and Christopher T. Seto\*



**Chiral, nonracemic (piperazin-2-yl)methanol derivatives with  $\sigma$ -receptor affinity**

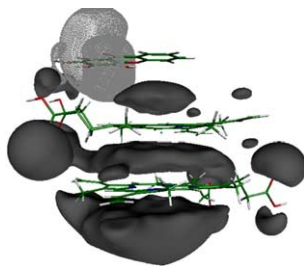
pp 3299–3311

Stephan Bedürftig and Bernhard Wünsch\*

**Definition of an electronic profile of compounds with inhibitory activity against hematin aggregation in malaria parasite**

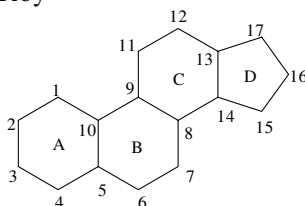
pp 3313–3321

César Portela, Carlos M. M. Afonso, Madalena M. M. Pinto and Maria João Ramos\*

**QSAR modeling of globulin binding affinity of corticosteroids using AM1 calculations**

pp 3323–3332

Kakali De, Chandana Sengupta and Kunal Roy\*

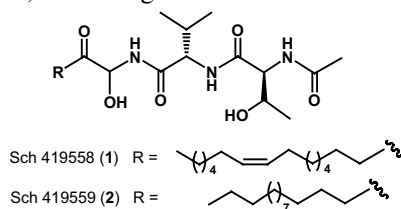


A QSAR study of binding affinity of a series of 30 steroids for corticosteroid-binding globulin was performed using Wang–Ford charges of the non-hydrogen common atoms obtained from molecular electrostatic potential surface of AM1 optimized energy-minimized geometries of the compounds. It was found from the study that the charges of different atoms of the steroid nucleus [atoms 3, 4, 5 (ring A), 8, 9 (fusion points of rings B and C) and 16 (ring D)] contribute significantly to the binding affinity.

**Two novel antibiotics, Sch 419558 and Sch 419559, produced by *Pseudomonas fluorescens*: effect on activity by overexpression of RpoE**

pp 3333–3338

Shu-Wei Yang,\* Ling Xu, Ronald Mierzwa, Ling He, Joseph Terracciano, Mahesh Patel, Vincent Gullo, Todd Black, Wenjun Zhao, Tze-Ming Chan and Min Chu\*

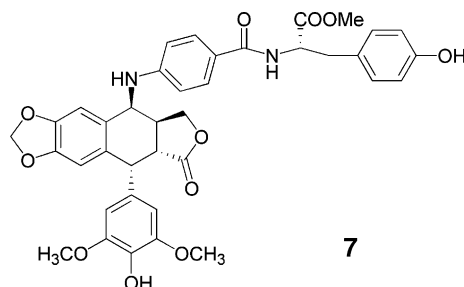


Two new RNA polymerase sigma-factor (RpoE) inhibitor, Sch 419558 (**1**) and Sch 419559 (**2**) were discovered from *Pseudomonas fluorescens*. Structures of **1** and **2** were elucidated by spectroscopic data analyses.

**Antitumor agents. Part 227: Studies on novel 4'-O-demethyl-epipodophyllotoxins as antitumor agents targeting topoisomerase II**

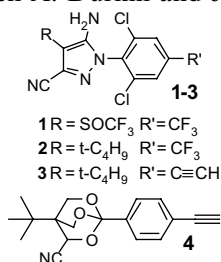
pp 3339–3344

Zhiyan Xiao, Kenneth F. Bastow, John R. Vance and Kuo-Hsiung Lee\*

**GABA receptor antagonists and insecticides: common structural features of 4-alkyl-1-phenylpyrazoles and 4-alkyl-1-phenyltrioxabicyclooctanes**

pp 3345–3355

Robert E. Sammelson, Pierluigi Caboni, Kathleen A. Durkin and John E. Casida\*

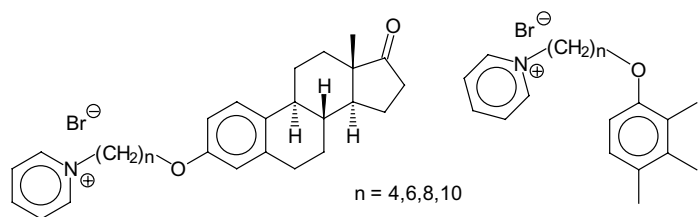


The major 1-phenylpyrazole insecticide **1** (fipronil) has common structural and biological features with *tert*-butyl and ethynyl analogs **2** and **3** and the conformationally similar and very potent trioxabicyclooctane **4**.

**ω-Pyridiniumalkylethers of steroidal phenols: new compounds with potent antibacterial and antiproliferative activities**

pp 3357–3362

C. Lange, N. Holzhey, B. Schönecker,\* R. Beckert, U. Möllmann and H.-M. Dahse

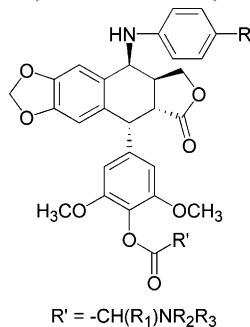


Antibacterial and antiproliferative activity in dependence on the alkyl chain length.

**Antitumor agents. Part 235: Novel 4'-ester etoposide analogues as potent DNA topoisomerase II inhibitors with improved therapeutic potential**

pp 3363–3369

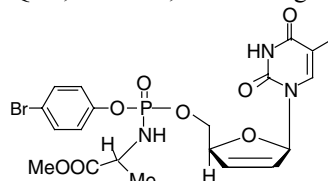
Zhiyan Xiao, John R. Vance, Kenneth F. Bastow, Arnold Brossi, Hui-Kang Wang and Kuo-Hsiung Lee\*



**Lipase-mediated stereoselective hydrolysis of stampidine and other phosphoramidate derivatives of stavudine**

pp 3371–3381

T. K. Venkatachalam, P. Samuel, G. Li, S. Qazi, C. Mao, S. Pendergrass and F. M. Uckun\*

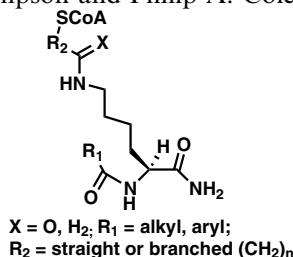


Stampidine and other halogen-substituted phosphoramidate derivatives of stavudine can be metabolized by lipase-mediated hydrolysis. Lipase showed chiral selectivity at the phosphorus center compared to esterase. Our results indicate that the lipase mediated formation of cyclic intermediate is the key step in the metabolism of stampidine and its analogs. Modeling studies and comparison of hydrolysis rate constants revealed chiral preference of the lipase active site for the putative 'S'-stereoisomer.

**Bisubstrate analogue structure–activity relationships for p300 histone acetyltransferase inhibitors**

pp 3383–3390

Vatsala Sagar, Weiping Zheng, Paul R. Thompson and Philip A. Cole\*



A series of depicted derivatives of Lys-CoA (X = O; R<sub>1</sub> = CH<sub>3</sub>; R<sub>2</sub> = CH<sub>2</sub>), our first reported selective inhibitor of p300 histone acetyltransferase, were designed, synthesized, and evaluated. The structure–activity relationship data generated have allowed for a greater understanding of the optimal requirements for potent inhibition of this key enzyme.

**QSAR and ADME**

pp 3391–3400

Corwin Hansch,\* Albert Leo, Suresh Babu Mekapati and Alka Kurup

The prediction from structure of ADME (absorption, distribution, metabolism, elimination) of drug candidates is an important goal to achieve since it can considerably reduce the cost of drug development. Using our database of 10,700 QSAR, we are now reaching the point where we can make many useful comparisons that illustrate how ADME is a practical way to describe the way organic compounds react with living systems. We also show that Caco-2 cells are useful to model absorption, but the most generally useful parameter is the octanol/water partition coefficient. It should be noted, however, that in our opinion, an in silico prediction of ADME is still a long way in the future.



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\*Corresponding author

Ⓜ<sup>+</sup> Supplementary data available via ScienceDirect

**COVER**

2004: Overlaps of the eight known aldolase alpha-beta barrels in 2-deoxyribose-5-phosphate aldolase (DERA). Ribbon model for DERA is shown in green, with key Lys residues capable of Schiff base formation highlighted in stick figure. Reactive Lys167 is shown in yellow. DeSantis, G.; Liu, J.; Clark, D. P.; Heine, A.; Wilson, I. A.; and Wong, C.-H. *Bioorganic & Medicinal Chemistry* 2003, 11, 43–52.



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