

Special Section: Symposium-in-Print

## Synthetic Ion Channels

Guest Editor: Ulrich Koert

*Fachbereich Chemie, Philipps-Universität Marburg, D-35032 Marburg, Germany*

### Contents

Bioorganic & Medicinal Chemistry Symposia-in-Print  
Foreword

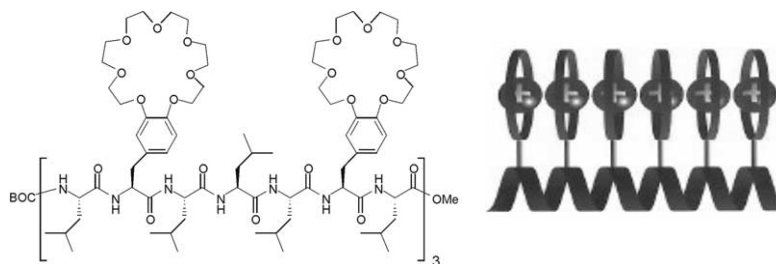
p 1275  
p 1277

#### SYMPOSIUM-IN-PRINT ARTICLES

**Design, synthesis, and characterization of peptide nanostructures having ion channel activity**

pp 1279–1290

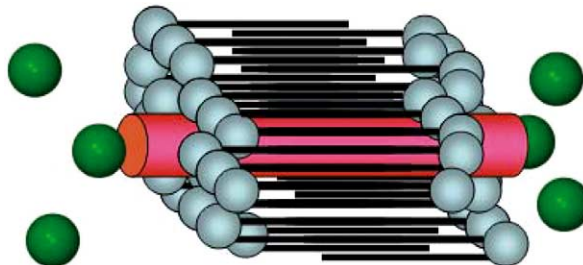
Eric Biron, François Otis, Jean-Christophe Meillon, Martin Robitaille, Julie Lamothe,  
Patrick Van Hove, Marie-Eve Cormier and Normand Voyer\*



**Functional, synthetic organic chemical models of cellular ion channels**

pp 1291–1304

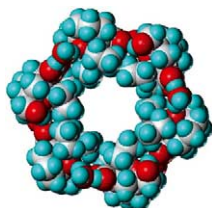
George W. Gokel,\* Paul H. Schlesinger, Natasha K. Djedović, Riccardo Ferdani,  
Egan C. Harder, Jiaxin Hu, W. Matthew Leevy, Jolanta Pajewska, Robert Pajewski  
and Michelle E. Weber



**Water molecules in hydroxy/acid networks as a competition between dynamics and bonding.  
Synthesis of a wet hydrophobic pore**

pp 1305–1314

Natalia Pérez-Hernández, Cirilo Pérez,\* Matías L. Rodríguez, Concepción Foces-Foces,\*  
Peter M. Tolstoy, Hans H. Limbach, Ezequiel Q. Morales, Ricardo Pérez and Julio D. Martín\*

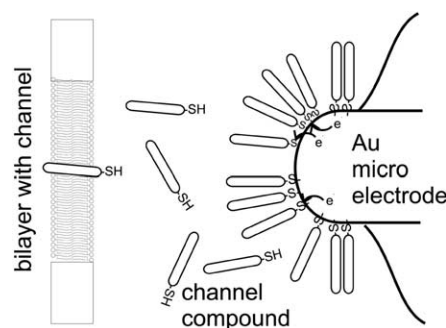


Compound ( $\pm$ )-**1n** gives, by way of the incorporation of water molecules, an efficient hexagonal assembly which extends to form a tubular H-bonding network.

**Electrochemical release from gold–thiolate electrodes for controlled insertion of ion channels into bilayer membranes**

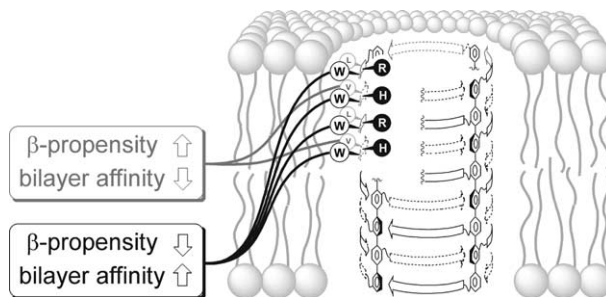
pp 1315–1324

M. B. Buchmann, T. M. Fyles\* and T. Sutherland

**Outer surface modification of synthetic multifunctional pores**

pp 1325–1336

Pinaki Talukdar, Naomi Sakai, Nathalie Sordé, David Gerard, Valérie M. F. Cardona  
and Stefan Matile\*

**Engineering charge selectivity in model ion channels**

pp 1337–1342

Tyler Lougheed, Zhihua Zhang, G. Andrew Woolley\* and Vitali Borisenko

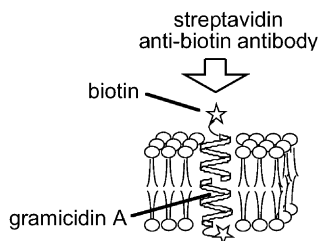


Charge selectivity in channels formed by covalently-linked alamethicin dimers was investigated through amino acid substitutions at position 18. Of the residues tested, lysine derivatives exhibited the greatest degree of anion selectivity. Pore diameter and the degree of counterion screening are proposed as key factors controlling the charge selectivity.

**Gramicidin-based channel systems for the detection of protein–ligand interaction**

pp 1343–1350

Shiroh Futaki,\* Youjun Zhang, Tatsuto Kiwada, Ikuhiko Nakase, Takeshi Yagami, Shigetoshi Oiki and Yukio Sugiura

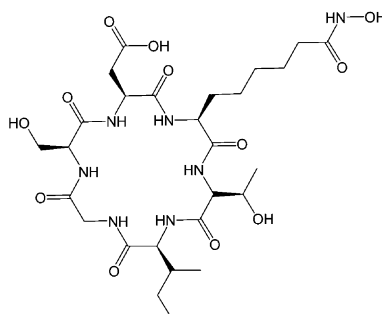


Interaction of the biotin with streptavidin or the anti-biotin antibody was monitored through the channel-current suppression of gramicidin.

**REGULAR ARTICLES****Toward an HDAC6 inhibitor: synthesis and conformational analysis of cyclic hexapeptide hydroxamic acid designed from  $\alpha$ -tubulin sequence**

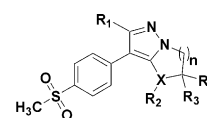
pp 1351–1356

Binoy Jose, Shinji Okamura, Tamaki Kato, Norikazu Nishino,\* Yuko Sumida and Minoru Yoshida

**Synthesis and selective cyclooxygenase-2 (COX-2) inhibitory activity of a series of novel bicyclic pyrazoles**

pp 1357–1366

Ramani R. Ranatunge,\* David S. Garvey, David R. Janero, L. Gordon Letts, Allison M. Martino, Madhavi G. Murty, Stewart K. Richardson, Delano V. Young and Irina S. Zemetseva



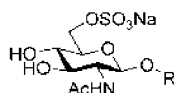
The synthesis of a series of novel bicyclic-pyrazoles and their in vitro cyclooxygenase-2 (COX-2) inhibitory activity in human whole blood (HWB) are reported.

$R_1$  = cyclohexyl, phenyl, benzyl  
 $R_2$  = H,  $CH_3$ ,  $COCH_3$ ,  $CH_2COO^tBu$ ,  $CH_2COOH$   
 $R_3$  = H,  $CH_3$   
 $X$  = O, N  
 $n$  = 1, 2

**Design of *N*-acetyl-6-sulfo- $\beta$ -D-glucosaminide-based inhibitors of influenza virus sialidase**

pp 1367–1375

Kenji Sasaki, Yoshihiro Nishida,\* Mikie Kambara, Hirotaka Uzawa, Tadanobu Takahashi, Takashi Suzuki, Yasuo Suzuki and Kazukiyo Kobayashi\*

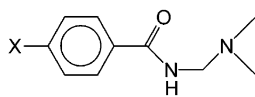


$R$  = *p*-nitrophenyl, naphthyl, propyl, glycerol

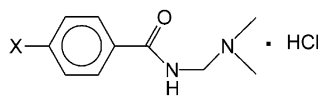
**QSPR/QSAR in *N*-[(dimethylamine)methyl] benzamides substituents groups influence upon electronic distribution and local anesthetics activity**

pp 1377–1381

Leoberto Costa Tavares\* and Antonia Tavares do Amaral



Set A



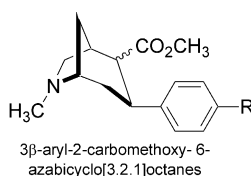
Set B

It was determined the carbonyl group frequency in the region of the infrared of *N*-[(dimethylamine)methyl] benzamides 4-substituted (set A) and their hydrochlorides (set B), that had its local anesthetic activity evaluated. The application of the Hammett equation considering the values of the absorption frequency of carbonyl group,  $\nu_{C=O}$ , using the electronic constants  $\sigma$ ,  $\sigma_1$ ,  $\sigma_R$ ,  $\chi$  and  $\mathfrak{R}$  leads to meaningful correlation. The nature and the contribution of substituent group electronic effects on the polarity of the carbonyl group was also analyzed. The use of the  $\nu_{C=O}$  as an experimental electronic parameter for QSPR studies was validated.

**2,3-Disubstituted 6-azabicyclo[3.2.1]octanes as novel dopamine transporter inhibitors**

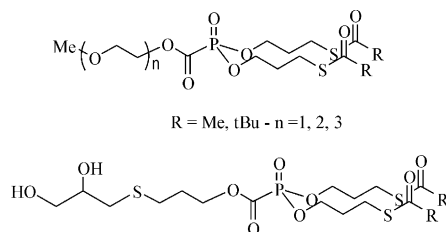
pp 1383–1391

Josefina Quirante,\* Xavier Vila, Josep Bonjoch, Alan P. Kozikowski and Kenneth M. Johnson


**Synthesis and in vitro evaluation of S-acyl-3-thiopropyl prodrugs of Foscarnet**

pp 1393–1402

Valérie Gagnard, Alain Leydet,\* Alain Morère, Jean-Louis Montero, Isabelle Lefèbvre, Gilles Gosselin, Christophe Pannecouque and Erick De Clercq

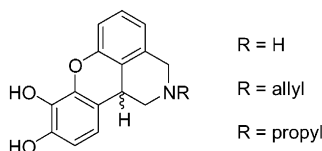


The PFA prodrugs were evaluated in vitro for their activity against human immunodeficiency viruses (HIV-1 and HIV-2).

**8,9-Dihydroxy-1,2,3,11b-tetrahydrochromeno[4,3,2-*de*]isoquinoline (dinoxyline), a high affinity and potent agonist at all dopamine receptor isoforms**

pp 1403–1412

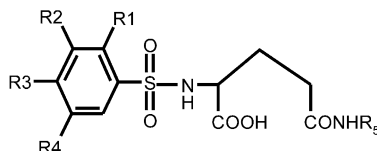
Russell A. Grubbs, Mechelle M. Lewis, Connie Owens-Vance, Elaine A. Gay, Amy K. Jassen, Richard B. Mailman and David E. Nichols\*



**5-*N*-Substituted-2-(substituted benzenesulphonyl) glutamines as antitumor agents. Part II: Synthesis, biological activity and QSAR study**

pp 1413–1423

Soma Samanta, K. Srikanth, Suchandra Banerjee, Bikash Debnath, Shovanlal Gayen and Tarun Jha\*

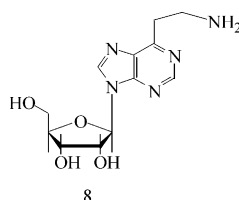


Synthesis, biological evaluation for % tumor cell count inhibition and QSAR study was performed using physicochemical and topological parameters on some 5-*N*-substituted-2-(substituted benzenesulphonyl)-glutamines as possible anticancer agents.

**Synthesis and biological evaluation of 6-substituted purine and 9-β-D-ribofuranosyl purine analogues**

pp 1425–1429

Jun-Feng Wang, Liang-Ren Zhang, Zhen-Jun Yang and Li-He Zhang\*

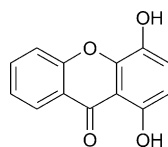


6-Substituted purine and 9-β-D-ribofuranosyl purine analogues were synthesized. Compound **8** exhibited middle inhibition on the growth of HeLa cells (70.21%) and HL-60 cells (70.85%) at 10 μM and the interaction with RNA.

**1,4-Dihydroxyxanthone modulates the adhesive property of endothelial cells by inhibiting intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) and E-selectin**

pp 1431–1437

Babita Madan, Ashok K. Prasad, Virinder S. Parmar and Balaram Ghosh\*

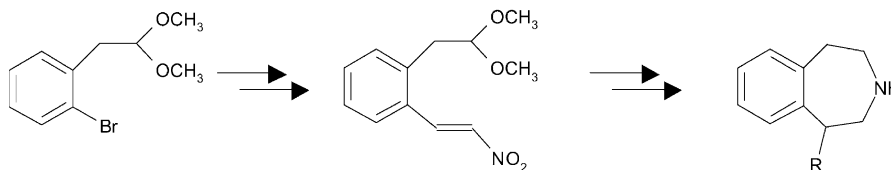


1,4-Dihydroxyxanthone modulates the adhesion of neutrophils to the human endothelial cell monolayer by inhibiting the expression of cell adhesion molecules, such as ICAM-1, VCAM-1 and E-selectin. The inhibition by 1,4-DHX is reversible and time dependent.

**Synthesis and structure/NMDA receptor affinity relationships of 1-substituted tetrahydro-3-benzazepines**

pp 1439–1451

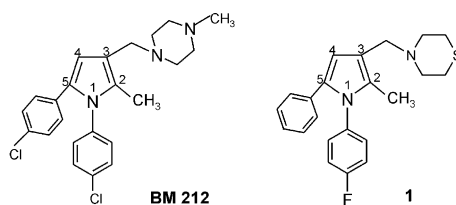
Olaf Krull and Bernhard Wünsch\*



**Antimycobacterial compounds. New pyrrole derivatives of BM212**

pp 1453–1458

Mariangela Biava,\* Giulio Cesare Porretta, Delia Deidda, Raffaello Pompei, Andrea Tafi and Fabrizio Manetti

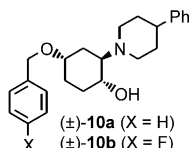


Previously we have identified **BM212** and **1**, two pyrrole derivatives with good in vitro activity against mycobacteria, on the base of a four-feature pharmacophore model individuated by us. These findings prompted us to prepare new pyrrole derivatives in the hope of increasing the activity. The microbiological data showed interesting in vitro activity against *Mycobacterium tuberculosis*.

**Synthesis of novel 4- and 5-substituted benzyl ether derivatives of vesamicol and in vitro evaluation of their binding properties to the vesicular acetylcholine transporter site**

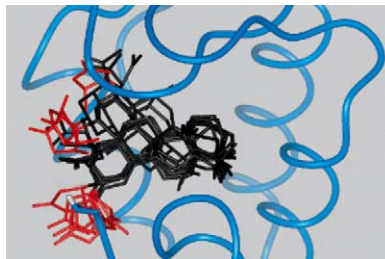
pp 1459–1465

Matthias Scheunemann,\* Dietlind Sorger, Barbara Wenzel, Katrin Heinitz, Reinhard Schliebs, Margrit Klingner, Osama Sabri and Jörg Steinbach

**Further insights on the structural aspects of PLA<sub>2</sub> inhibition by  $\gamma$ -hydroxybutenolide-containing natural products: a comparative study on petrosaspongiolides M–R**

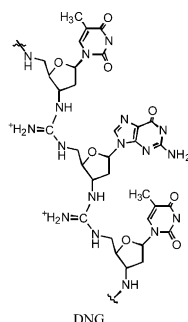
pp 1467–1474

Maria Chiara Monti, Agostino Casapullo, Raffaele Riccio and Luigi Gomez-Paloma\*

**Deoxynucleic guanidine: synthesis and incorporation of purine nucleosides into positively charged DNG oligonucleotides**

pp 1475–1481

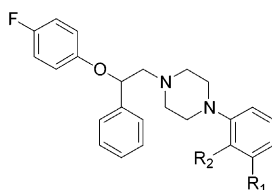
Hemavathi Challa and Thomas C. Bruice\*



## Synthesis and biological evaluation of 2-(4-fluorophenoxy)-2-phenyl-ethyl piperazines as serotonin-selective reuptake inhibitors with a potentially improved adverse reaction profile

pp 1483–1491

James M. Dorsey, Maria G. Miranda, Nicholas V. Cozzi and Kevin G. Pinney\*

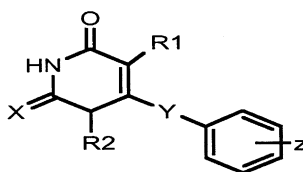


- 7  $R_1 = \text{Cl}, R_2 = \text{H}$   
 8  $R_1 = \text{H}, R_2 = \text{OCH}_3$   
 9  $R_1 = \text{CF}_3, R_2 = \text{H}$

## QSAR study on some anti-HIV HEPT analogues using physicochemical and topological parameters

pp 1493–1503

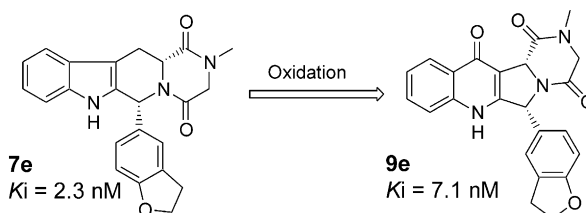
Shovanlal Gayen, Bikash Debnath, Soma Samanta and Tarun Jha\*



## Synthesis and SAR of tetracyclic pyrroloquinolones as phosphodiesterase 5 inhibitors

pp 1505–1515

Weiqin Jiang,\* Vernon C. Alford, Yuhong Qiu, Sheela Bhattacharjee, T. Matthew John, Donna Haynes-Johnson, Patricia J. Kraft, Scott G. Lundeen and Zhihua Sui\*



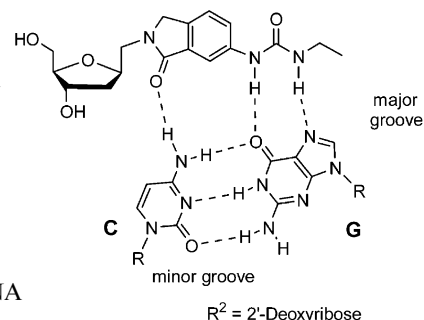
Synthesis of pyrroloquinolones **9a–9i** and their biological activities towards PDE5 were described.

## Synthesis and duplex DNA recognition studies of oligonucleotides containing a ureido isoindolin-1-one homo-*N*-nucleoside. A comparison of host–guest and DNA recognition studies

pp 1517–1526

Eric Mertz, Sebastiano Mattei and Steven C. Zimmerman\*

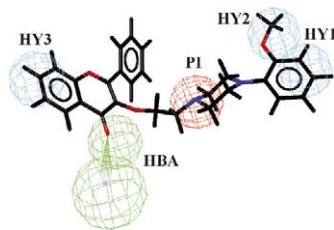
In an effort to construct non-natural bases to be used in triplex-based antigene DNA recognition strategies, a ureido-isoindolin-1-one homo-*N*-nucleoside base was designed to bind the cytosine-guanine (CG) base pair. An organic soluble analogue of this base was shown to effectively complex CG ( $K_{\text{assoc}} = 740 \text{ M}^{-1}$ ) in chloroform through formation of three hydrogen bonds (Mertz, E.; Mattei, S.; Zimmerman, S. C. *Org. Lett.* **2000**, 2, 2931–2934). The novel nucleoside base was synthesized and successfully incorporated into oligonucleotides which were used in triple helix melting temperature studies. Low melting temperatures were observed when the isoindolin-1-one base was paired opposite CG as well as GC, TA, and AT, thus indicating that despite favorable recognition in model studies, the artificial base did not effectively recognize duplex DNA to form pyrimidine-purine-pyrimidine type triple helices.



**Design, synthesis, and  $\alpha_1$ -adrenoceptor binding properties of new arylpiperazine derivatives bearing a flavone nucleus as the terminal heterocyclic molecular portion**

pp 1527–1535

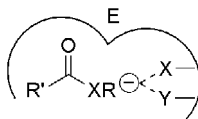
Laura Betti, Monia Floridi, Gino Giannaccini, Fabrizio Manetti,\* Chiara Paparelli, Giovannella Strappaghetti\* and Maurizio Botta



**Kinetic and structural consequences of the leaving group in substrates of a class C  $\beta$ -lactamase**

pp 1537–1542

Yong-Mo Ahn and R. F. Pratt\*

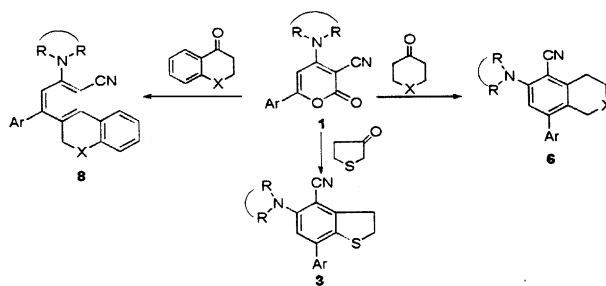


Optimization of interactions between the anionic leaving group and the enzyme active site.

**Synthesis of bicyclic biaryls as glucose-6-phosphatase inhibitors**

pp 1543–1549

Farhanullah, Brajendra K. Tripathi, Arvind K. Srivastava and Vishnu Ji Ram\*

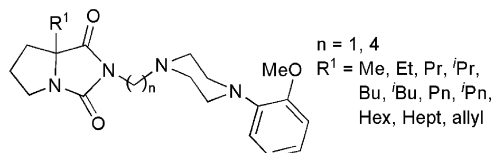


Synthesis of bicyclic biaryls as glucose-6-phosphatase inhibitors is described.

**Synthesis and structure–activity relationships of a new model of arylpiperazines. Part 7: Study of the influence of lipophilic factors at the terminal amide fragment on 5-HT<sub>1A</sub> affinity/selectivity**

pp 1551–1557

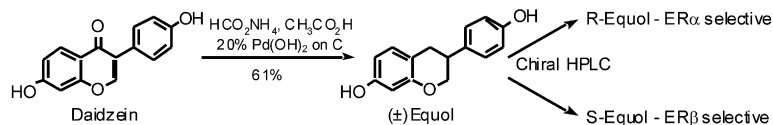
María L. López-Rodríguez,\* David Ayala, Alma Viso, Bellinda Benhamú, Roberto Fernández de la Pradilla, Fernando Zarza and José A. Ramos





**Equol, a natural estrogenic metabolite from soy isoflavones: convenient preparation and resolution of *R*- and *S*-equols and their differing binding and biological activity through estrogen receptors alpha and beta****pp 1559–1567**

Rajeev S. Muthyala, Young H. Ju, Shubin Sheng, Lee D. Williams, Daniel R. Doerge, Benita S. Katzenellenbogen, William G. Helferich\* and John A. Katzenellenbogen\*



(±)-Equol was prepared in one step from daidzein and separated into enantiomers by chiral HPLC. Binding and transcriptional activity through estrogen receptors  $\alpha$  and  $\beta$  was determined.

**OTHER CONTENTS**

Corrigendum  
Contributors to this issue  
Instructions to contributors

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\*Corresponding author

**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 & Medical Chemistry* 2003, 11, 43–52.



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