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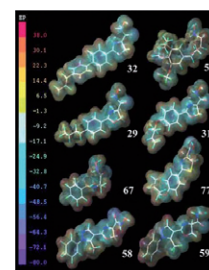
ARTICLES

**Pharmacophoric features of *Pseudomonas aeruginosa* deacetylase LpxC inhibitors:  
An electronic and structural analysis**

pp 861–868

Rameshwar U. Kadam, Archana Chavan and Nilanjan Roy\*

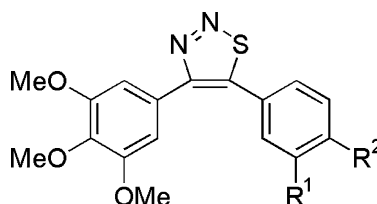
An electronic and structural analysis of *Pseudomonas aeruginosa* Deacetylase LpxC inhibitors reveals characteristic pharmacophoric features of these inhibitors, which are useful for in-depth understanding of inhibitors-enzyme interaction and designing more potent inhibitors against this target.



**Synthesis and activity of Combretastatin A-4 analogues: 1,2,3-thiadiazoles as potent antitumor agents**

pp 869–873

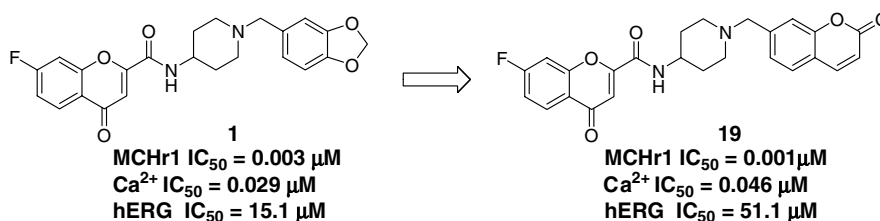
Maojiang Wu, Qiming Sun, Chunhao Yang,\* Dongdong Chen, Jian Ding,\* Yi Chen, Liping Lin and Yuyuan Xie



**An evaluation of 3,4-methylenedioxy phenyl replacements in the aminopiperidine  
chromone class of MCHR1 antagonists**

pp 874–878

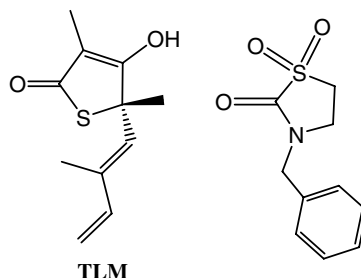
Rajesh R. Iyengar,\* John K. Lynch, Mathew M. Mulhern, Andrew S. Judd, Jennifer C. Freeman, Ju Gao, Andrew J. Souers, Gang Zhao, Dariusz Wodka, H. Doug Falls, Sevan Brodjian, Brian D. Dayton, Regina M. Reilly, Sue Swanson, Zhi Su, Ruth L. Martin, Sandra T. Leitza, Kathryn A. Houseman, Gilbert Diaz, Christine A. Collins, Hing L. Sham and Philip R. Kym



**Synthesis and biological evaluation of thiazolidine-2-one 1,1-dioxide as inhibitors of *Escherichia coli*  $\beta$ -ketoacyl-ACP-synthase III (FabH)**

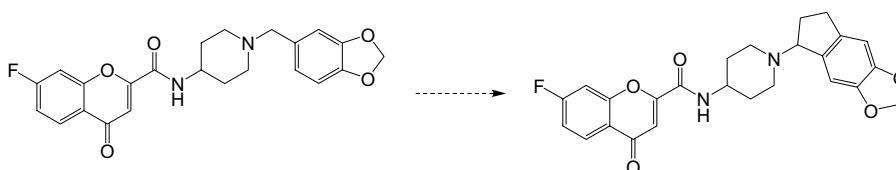
pp 879–883

Mamoun M. Alhamadsheh, Norman C. Waters, Donald P. Huddler, Mara Kreishman-Deitrick, Galina Florova and Kevin A. Reynolds\*


**Constrained 7-fluorocarboxychromone-4-aminopiperidine based Melanin-concentrating hormone receptor 1 antagonists: The effects of chirality on substituted indan-1-ylamines**

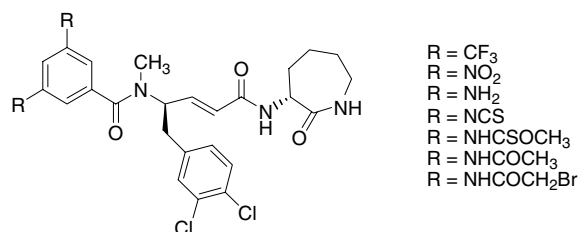
pp 884–889

Andrew J. Souers,\* Rajesh R. Iyengar, Andrew S. Judd, David W. A. Beno, Ju Gao, Gang Zhao, Michael E. Brune, James J. Napier, Mathew M. Mulhern, John K. Lynch, Jennifer C. Freeman, Dariusz Wodka, Chong J. Chen, H. Doug Falls, Sevan Brodjian, Brian D. Dayton, Gilbert J. Diaz, Eugene N. Bush, Robin Shapiro, Brian A. Droz, Victoria Knourek-Segel, Lisa E. Hernandez, Kennan C. Marsh, Regina M. Reilly, Hing L. Sham, Christine A. Collins and Philip R. Kym


**Design and synthesis of 3,5-disubstituted benzamide analogues of DNK333 as dual NK<sub>1</sub>/NK<sub>2</sub> receptor probes**

pp 890–894

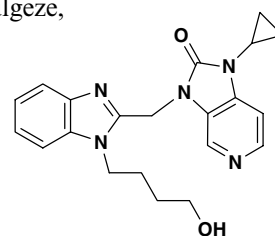
Venkat Manoj Swarna, Bradley J. Udem and Vijaya L. Korlipara\*


 Here we report the synthesis of a series of DNK333 derivatives. The 3,5-dinitro derivative of DNK333 was found to possess potent and balanced dual NK<sub>1</sub>/NK<sub>2</sub> receptor antagonist activities in the functional assay using guinea pig trachea.

**Respiratory syncytial virus fusion inhibitors. Part 4: Optimization for oral bioavailability**

pp 895–901

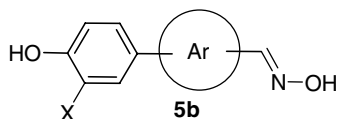
Kuo-Long Yu, Ny Sin, Rita L. Civiello, X. Alan Wang, Keith D. Combrink, H. Belgin Gulgeze, Brian L. Venables, J. J. Kim Wright, Richard A. Dalterio, Lisa Zadjura, Anthony Marino, Sandra Dando, Celia D'Arienzo, Kathleen F. Kadow, Christopher W. Cianci, Zhufang Li, Junius Clarke, Eugene V. Genovesi, Ivette Medina, Lucinda Lamb, Richard J. Colonna, Zheng Yang, Mark Krystal and Nicholas A. Meanwell\*

 A series of benzimidazole-based inhibitors of respiratory syncytial virus (RSV) fusion were optimized for antiviral potency, membrane permeability and metabolic stability in human liver microsomes. 1-Cyclopropyl-1,3-dihydro-3-[[1-(4-hydroxybutyl)-1*H*-benzimidazol-2-yl]methyl]-2*H*-imidazo[4,5-*c*]pyridin-2-one (**6m**, BMS-433771) was identified as a potent RSV inhibitor demonstrating good bioavailability in the mouse, rat, dog and cynomolgus monkey that demonstrated antiviral activity in the BALB/c and cotton rat models of infection following oral administration.

**6m, BMS-433771**

**ER $\beta$  ligands. Part 5: Synthesis and structure–activity relationships of a series of 4'-hydroxyphenyl-aryl-carbaldehyde oxime derivatives**

pp 902–906

Richard E. Mewshaw,\* S. Marc Bowen, Heather A. Harris, Zhang B. Xu, Eric S. Manas and Stephen T. Cohn

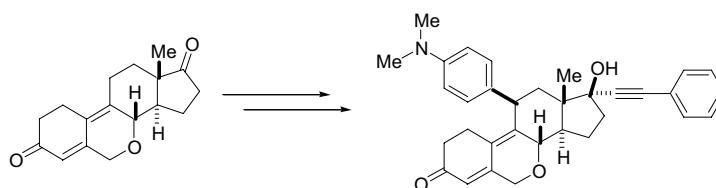


A series of 4'-hydroxyphenyl-aryl-carbaldehyde oximes (**5b**) was prepared and found to have high-affinity (4 nM) and modest selectivity (39-fold) for estrogen receptor- $\beta$ .

**Synthesis and identification of novel oxa-steroids as progesterone receptor antagonists**

pp 907–910

Fu-An Kang,\* George Allan, Jihua Guan, Nareshkumar Jain, Olivia Linton, Pamela Tannenbaum, Jun Xu, Peifang Zhu, Joseph Gunnet, Xin Chen, Keith Demarest, Scott Lundeen and Zhihua Sui

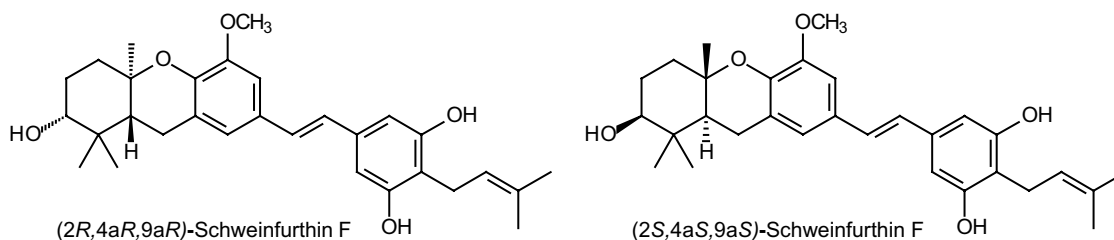


Novel 7-oxa-steroids were synthesized and identified as new potent and selective progesterone receptor antagonists.

**Total synthesis of (*R,R,R*)- and (*S,S,S*)-schweinfurthin F: Differences of bioactivity in the enantiomeric series**

pp 911–915

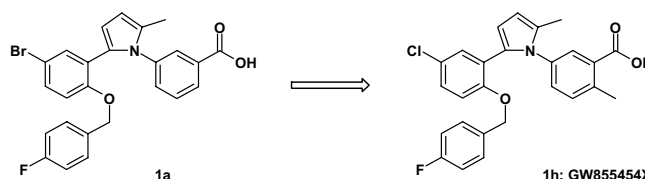
Nolan R. Mente, Andrew J. Wiemer, Jeffrey D. Neighbors, John A. Beutler, Raymond J. Hohl and David F. Wiemer\*

**1,5-Biaryl pyrrole derivatives as EP<sub>1</sub> receptor antagonists. Structure–activity relationships of 6-substituted and 5,6-disubstituted benzoic acid derivatives**

pp 916–920

Adrian Hall,\* Susan H. Brown, Iain P. Chessell, Anita Chowdhury, Nicholas M. Clayton, Tanya Coleman, Gerard M. P. Giblin, Beverley Hammond, Mark P. Healy, Matthew R. Johnson, Ann Metcalf, Anton D. Michel, Alan Naylor, Riccardo Novelli, David J. Spalding, Jennifer Sweeting and Lisa Winyard

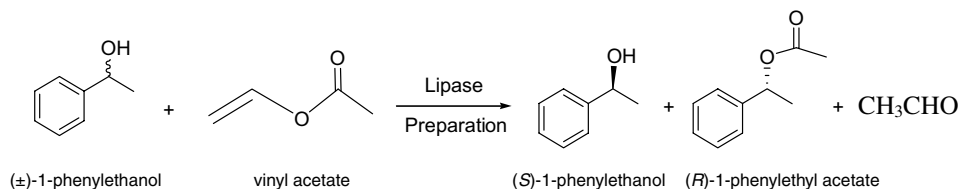
Substitution of the benzoic acid moiety of compounds such as **1a** led to the identification of **1h**, which was active in the established FCA model of inflammatory pain and showed good pharmacokinetics in the rat.



**Kinetic resolution of ( $\pm$ )-1-phenylethanol in [Bmim][PF<sub>6</sub>] using high activity preparations of lipases**

pp 921–924

Shweta Shah and Munishwar N. Gupta\*

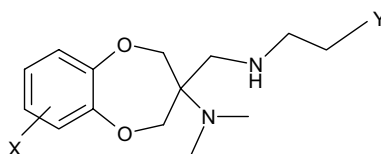


It is shown that high activity preparations of the lipases are far superior to the lyophilized powders in kinetic resolution of ( $\pm$ )-1-phenylethanol in [Bmim][PF<sub>6</sub>].

**1,5-Benzodioxepin derivatives as a novel class of muscarinic M<sub>3</sub> receptor antagonists**

pp 925–931

Shuji Sonda,\* Kenichi Katayama, Masakazu Fujio, Hiroshi Sakashita, Kenichi Inaba, Kiyoshi Asano and Toshiaki Akira

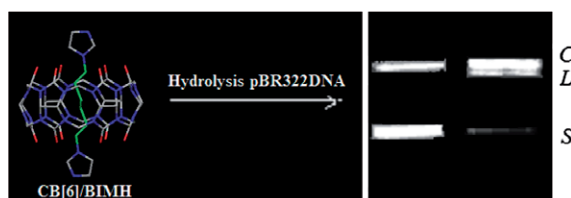


The structure–activity relationships of novel 1,5-benzodioxepin derivatives as muscarinic M<sub>1</sub>–M<sub>3</sub> receptor antagonists are reported.

**The crystal structure, self-assembly, DNA-binding and cleavage studies of the [2]pseudorotaxane composed of cucurbit[6]uril**

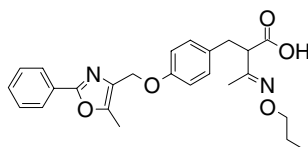
pp 932–936

Fang-Jun Huo, Cai-Xia Yin and Pin Yang\*

**Design and synthesis of oxime ethers of  $\alpha$ -acyl- $\beta$ -phenylpropanoic acids as PPAR dual agonists**

pp 937–941

Hee Oon Han, Seung Hae Kim, Kyoung-Hee Kim, Gwong-Cheung Hur, Hyeon Joo Yim, Hee-Kyung Chung, Sung Ho Woo, Ki Dong Koo, Chang-Seok Lee, Jong Sung Koh\* and Geun Tae Kim\*

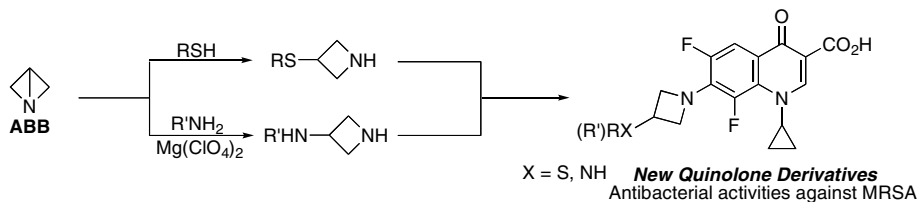
**111**

Compound **111** exhibited potent in vitro activities in PPAR $\alpha$  and  $\gamma$  (EC<sub>50</sub> = 19, 13 nM). It showed better glucose lowering effect than rosiglitazone as well.

**Synthesis and antibacterial activities of new quinolone derivatives utilizing 1-azabicyclo[1.1.0]butane**

pp 942–945

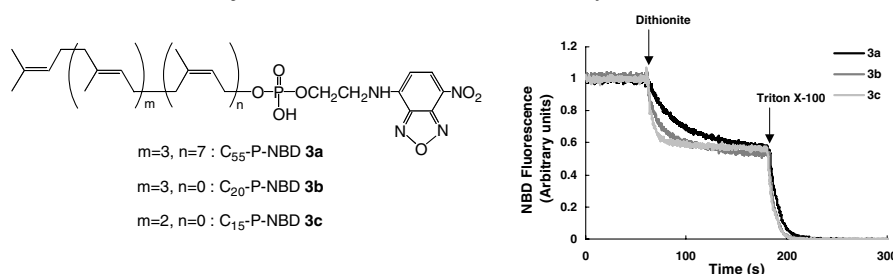
Yoshifumi Ikee, Kana Hashimoto, Masaaki Nakashima, Kazuhiko Hayashi, Shigeki Sano, Motoo Shiro and Yoshimitsu Nagao\*



**Novel fluorescent analogues for transmembrane movement study of polyprenyl phosphates**

pp 946–950

Koichi Koseki, Satoshi Yamashita, Seiji Takahashi and Tanetoshi Koyama\*

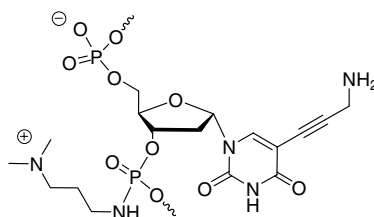


Novel NBD-labeled fluorescent polyprenyl phosphate analogues were synthesized for transmembrane movement study of polyprenyl phosphates, which may promise a methodology for the direct observation of the lipids flip-flop.

**5-Propynylamino  $\alpha$ -deoxyuridine promotes DNA duplex stabilization of anionic and neutral but not cationic  $\alpha$ -oligonucleotides**

pp 951–954

Gaëlle Deglane, François Morvan, Françoise Debart and Jean-Jacques Vasseur\*



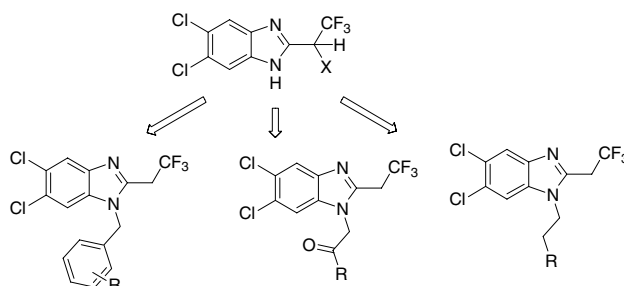
Incorporation of 5-propynylamino and 5-propynyl  $\alpha$ -2'-deoxyuridine into  $\alpha$ -oligonucleotides ( $\alpha$ -ON) allows high-affinity targeting of complementary DNA for anionic and neutral but not for cationic  $\alpha$ -ON.



**2-(2,2,2-Trifluoroethyl)-5,6-dichlorobenzimidazole derivatives as potent androgen receptor antagonists**

pp 955–958

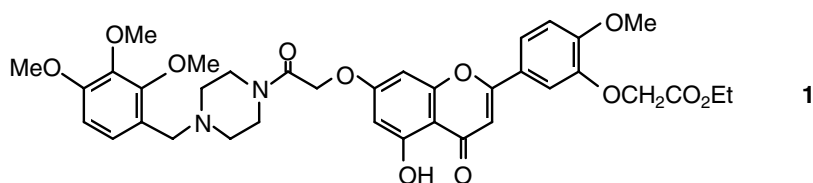
Raymond A. Ng, Jihua Guan, Vernon C. Alford, Jr., James C. Lanter, George F. Allan, Tifanie Sbriscia, Scott G. Lundeen and Zhihua Sui\*



**Synthesis and antimalarial evaluation of a series of piperazinyl flavones**

pp 959–963

Gwenola Auffret, Mehdi Labaied, François Frappier, Philippe Rasoanaivo, Philippe Grellier and Guy Lewin\*

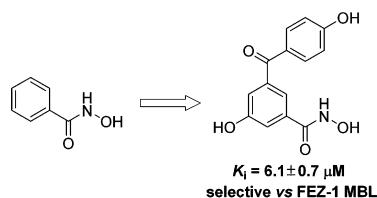


Most of 27 synthesized piperazinyl flavones displayed micromolar in vitro inhibition of *Plasmodium falciparum*, including **1** also active when given orally to *Plasmodium yoelii nigeriensis* infected mice.

**Inhibitors of the FEZ-1 metallo-β-lactamase**

pp 964–968

Benoît M. R. Liénard, Louise E. Horsfall, Moreno Galleni, Jean-Marie Frère and Christopher J. Schofield\*

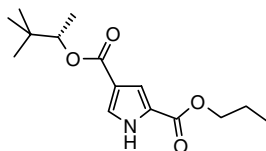


The development of a FEZ-1 metallo-β-lactamase inhibitor.

**<sup>13</sup>C bis-labeled pyrroles: A tool for the identification of the rat metabolism of 3-methyl pyrrole-2,4-dicarboxylic acid 2-propyl ester 4-(1,2,2-trimethyl-propyl) ester**

pp 969–973

Fabrizio Micheli,\* Paolo Cavanni, Romano Di Fabio, Daniele Donati, Mahmoud Hamdan, Stefano Provera, Maria Elvira Tranquillini and Giovanni Vitulli



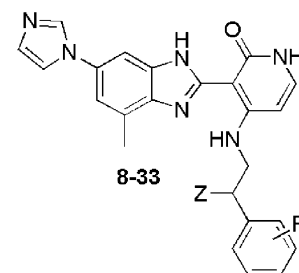
Investigation on the metabolic fate of the pyrrole mGluR1 antagonist class is presented.

**Novel 1H-(benzimidazol-2-yl)-1H-pyridin-2-one inhibitors of insulin-like growth factor I (IGF-1R) kinase**

pp 974–977

Mark D. Wittman,\* Balu Balasubramanian, Karen Stoffan, Upender Velaparthy, Pieying Liu, Subramaniam Krishnanathan, Joan Carboni, Aixin Li, Ann Greer, Ricardo Attar, Marco Gottardis, Chiehying Chang, Bruce Jacobson, Yax Sun, Steven Hansel, Mary Zoekler and Dolatrai M. Vyas

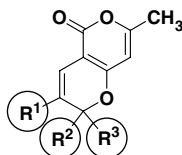
A novel class of benzimidazole–pyridone inhibitors of insulin-like growth factor I (IGF-1R) kinase is described.



**Efficient synthesis of substituted 7-methyl-2*H*,5*H*-pyrano[4,3-*b*]pyran-5-ones and evaluation of their *in vitro* antiproliferative/cytotoxic activities**

pp 978–982

Heiko Leutbecher, Lawrence A. D. Williams, Harald Rösner and Uwe Beifuss\*

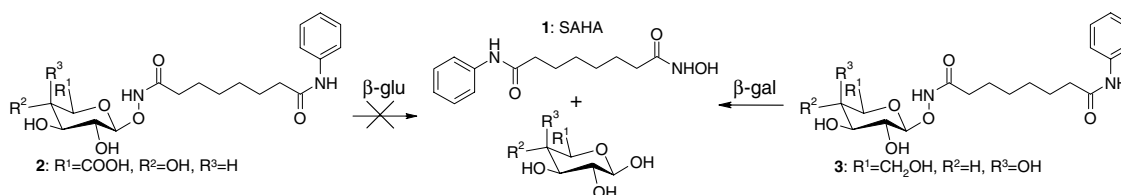


The title compounds were synthesized efficiently. Their *in vitro* antiproliferative/cytotoxic activity was evaluated with human SH-SY5Y neuroblastoma cells. IC<sub>50</sub> values are ranging from 6.7 to >200 μM.

**Synthesis and biological evaluation of the suberoylanilide hydroxamic acid (SAHA) β-glucuronide and β-galactoside for application in selective prodrug chemotherapy**

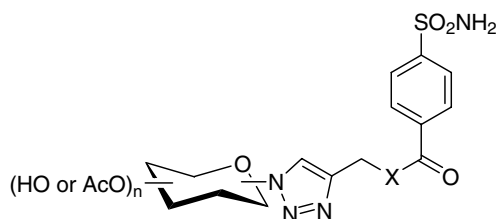
pp 983–986

Mickaël Thomas, Freddy Rivault, Isabelle Tranoy-Opalinski, Joëlle Roche, Jean-Pierre Gesson and Sébastien Papot\*

**Inhibition of membrane-associated carbonic anhydrase isozymes IX, XII and XIV with a library of glycoconjugate benzenesulfonamides**

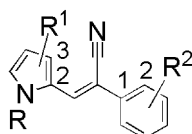
pp 987–992

Brendan L. Wilkinson, Laurent F. Bornaghi, Todd A. Houston, Alessio Innocenti, Daniela Vullo, Claudiu T. Supuran\* and Sally-Ann Poulsen\*

**Discovery of (*Z*)-2-phenyl-3-(1*H*-pyrrol-2-yl)acrylonitrile derivatives active against *Haemonchus contortus* and *Ctenocephalides felis* (cat flea)**

pp 993–997

Abdelselam Ali, Marianne Bliese, Jo-Anne M. Rasmussen, Roger M. Sargent, Simon Saubern, David G. Sawutz, John S. Wilkie, David A. Winkler, Kevin N. Winzenberg\* and Ruth C. J. Woodgate

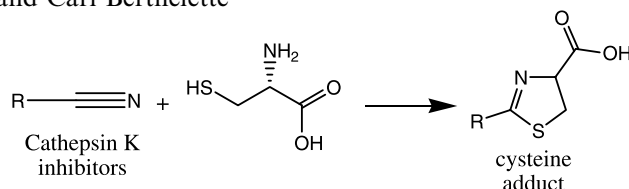


We describe the synthesis of a set of (*Z*)-2-phenyl-3-(1*H*-pyrrol-2-yl)acrylonitrile derivatives and the *in vitro* screening of these compounds against the animal parasites *Haemonchus contortus* and *Ctenocephalides felis*.

### A generally applicable method for assessing the electrophilicity and reactivity of diverse nitrile-containing compounds

pp 998–1002

Renata M. Oballa,\* Jean-François Truchon, Christopher I. Bayly, Nathalie Chauret, Stephen Day, Sheldon Crane and Carl Berthelette

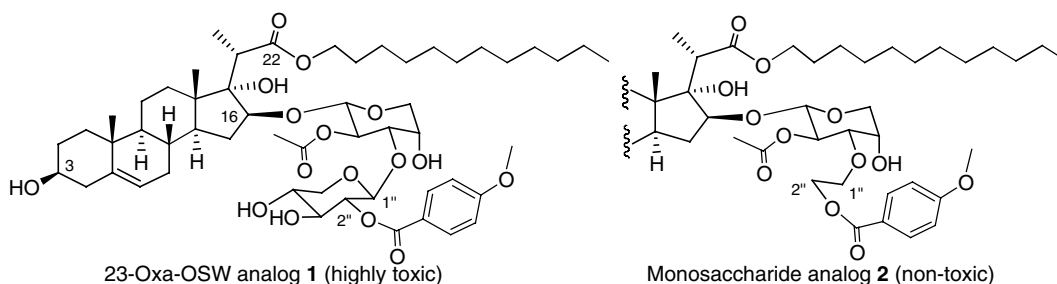


A simple theoretical calculation (reactivity of nitriles with methanethiol) was used to predict the electrophilicity of diverse nitrile warheads. These calculated electrophilicities were found to correlate with the extent of thiazoline adduct formed upon incubation of the nitriles with cysteine.

### Synthesis of OSW saponin analogs with modified sugar residues and their antiproliferative activities

pp 1003–1007

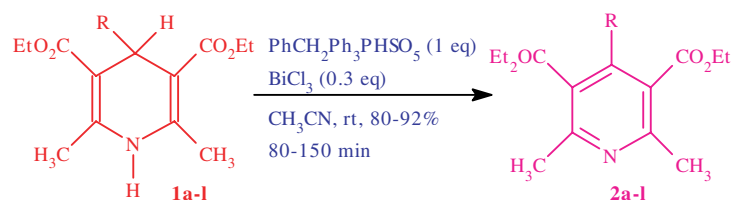
Pingping Tang, Fatemah Mamdani, Xiaoyi Hu, Jun O. Liu and Biao Yu\*



### A convenient and efficient protocol for oxidative aromatization of Hantzsch 1,4-dihydropyridines using benzyltriphenylphosphonium peroxymonosulfate under almost neutral reaction conditions

pp 1008–1012

Hadi Adibi\* and Abdol Reza Hajipour

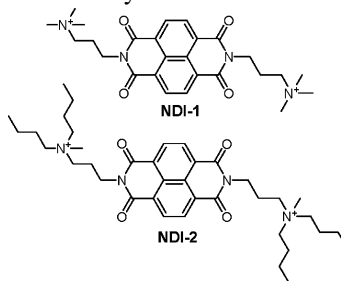


Aromatization of 1,4-dihydropyridines **1a-I** to the corresponding pyridine derivatives **2a-I** has been studied using benzyltriphenylphosphonium peroxymonosulfate **BTPPMS** in the presence of  $\text{BiCl}_3$  at ambient temperature.

### Binding mode and affinity studies of DNA-binding agents using topoisomerase I DNA unwinding assay

pp 1013–1017

Ruel E. McKnight,\* Aaron B. Gleason, James A. Keyes and Sadia Sahabi



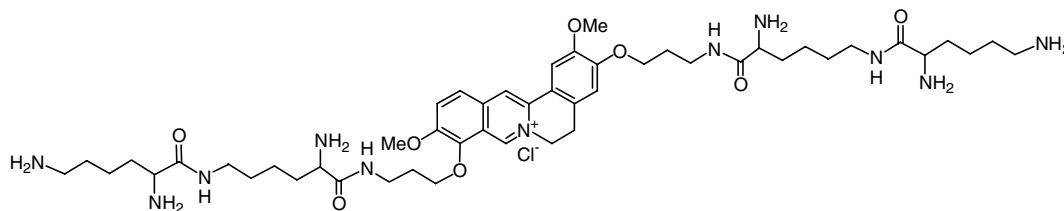
Topoisomerase I unwinding assay is used to determine the relative DNA-binding affinities of homologous naphthalene diimides as well as the binding mode adopted by several known DNA-binding agents.



**Amplification of DNA-binding affinities of protoberberine alkaloids by appended polyamines**

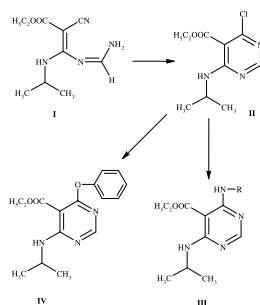
pp 1018–1021

Ji-Yan Pang, Yu-Hua Long, Wen-Hua Chen\* and Zhi-Hong Jiang

**Synthesis and biological evaluation of some 5-ethoxycarbonyl-6-isopropylamino-4-(substitutedphenyl) aminopyrimidines as potent analgesic and anti-inflammatory agents**

pp 1022–1024

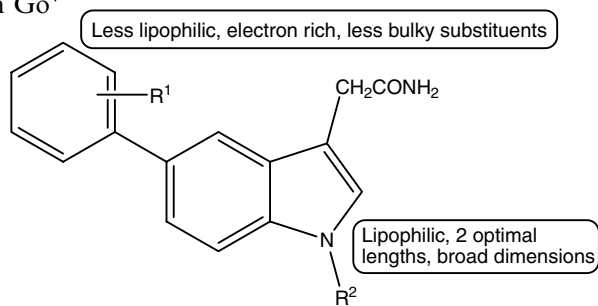
Mahesh T. Chhabria,\* Hardik G. Bhatt, Hitesh G. Raval and Pratik M. Oza

**Quantitative structure–activity relationship (QSAR) of indoloacetamides as inhibitors of human isoprenylcysteine carboxyl methyltransferase**

pp 1025–1032

Jo-Lene Leow, Rudi Baron, Patrick J. Casey and Mei-Lin Go\*

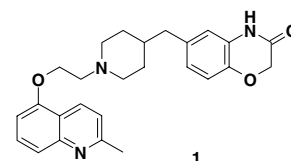
QSAR of the ICMT inhibitory activities of indoloacetamides showed contrasting steric and lipophilic preferences for the N-substituent and the substituted phenyl ring.

**3,4-Dihydro-2H-benzoxazinones as dual-acting 5-HT<sub>1A</sub> receptor antagonists and serotonin reuptake inhibitors**

pp 1033–1036

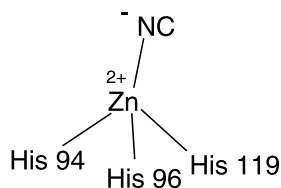
Peter J. Lovell,\* Frank E. Blaney, Caroline J. Goodacre, Claire M. Scott, Paul W. Smith, Kathryn R. Starr, Kevin M. Thewlis, Antonio K. K. Vong, Simon E. Ward and Jeannette M. Watson

Investigation of halogen substitution in lead compound **1** has led to the identification of analogues which combine high affinity for 5-HT<sub>1A</sub> receptors and potent serotonin reuptake inhibitory activity. Several compounds show an improved selectivity over 5-HT<sub>1B</sub> and 5-HT<sub>1D</sub> receptors and a superior pharmacokinetic profile in the rat.



**Carbonic anhydrase inhibitors. Inhibition studies of the human secretory isoform VI with anions**  
Isao Nishimori, Alessio Innocenti, Daniela Vullo, Andrea Scozzafava and Claudiu T. Supuran\*

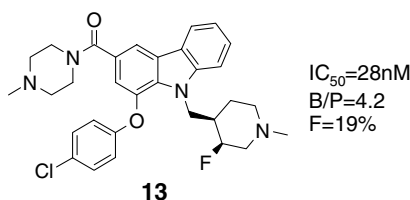
pp 1037–1042



**Novel carbazole derivatives as NPY Y1 antagonists**

pp 1043–1046

Colin P. Leslie,\* Romano Di Fabio,\* Francesca Bonetti, Manuela Borriello, Simone Braggio, Giovanna Dal Forno, Daniele Donati, Alessandro Falchi, Damiano Ghirlanda, Riccardo Giovannini, Francesca Pavone, Angelo Pecunioso, Giorgio Pentassuglia, Domenica A. Pizzi, Giovanna Rumboldt and Luigi Stasi



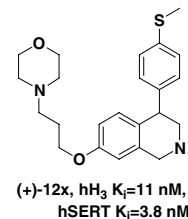
A series of carbazoles showing antagonist activity at the NPY Y1 receptor were prepared and characterised. Compound **13** combines potent activity with good brain penetration and modest bioavailability.

**Novel tetrahydroisoquinolines are histamine H<sub>3</sub> antagonists and serotonin reuptake inhibitors**

pp 1047–1051

Michael A. Letavic,\* John M. Keith, Jill A. Jablonowski, Emily M. Stocking, Leslie A. Gomez, Kiev S. Ly, Jennifer M. Miller, Ann J. Barbier, Pascal Bonaventure, Jamin D. Boggs, Sandy J. Wilson, Kirsten L. Miller, Brian Lord, Heather M. McAllister, D. J. Tognarelli, Jiejun Wu, Marta C. Abad, Carsten Schubert, Timothy W. Lovenberg and Nicholas I. Carruthers

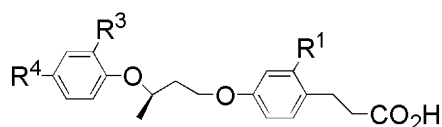
Novel histamine H<sub>3</sub> antagonists with serotonin reuptake activity are reported.



**Design and synthesis of a novel class of dual PPAR $\gamma$ / $\delta$  agonists**

pp 1052–1055

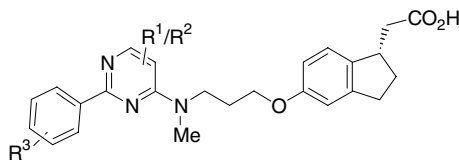
Isabel C. Gonzalez,\* Jason Lamar, Fatima Iradier, Yanping Xu, Leonard L. Winneroski, Jeremy York, Nathan Yumibe, Richard Zink, Chahrzad Montrose-Rafizadeh, Gary J. Etgen, Carol L. Broderick, Brian A. Oldham and Nathan Mantlo



**Indanylacetic acid derivatives carrying aryl-pyridyl and aryl-pyrimidinyl tail groups—new classes of PPAR  $\gamma/\delta$  and PPAR  $\alpha/\gamma/\delta$  agonists**

pp 1056–1061

Louis-David Cantin,\* Sidney Liang, Herbert Ogutu, Christiana I. Iwuagwu, Ken Boakye, William H. Bullock, Michael Burns, Roger Clark, Thomas Claus, Fernando E. delaCruz, Michelle Daly, Frederick J. Ehrigott, Jeffrey S. Johnson, Christine Keiper, James N. Livingston, Robert W. Schoenleber, Jeffrey Shapiro, Christopher Town, Ling Yang, Manami Tsutsumi and Xin Ma



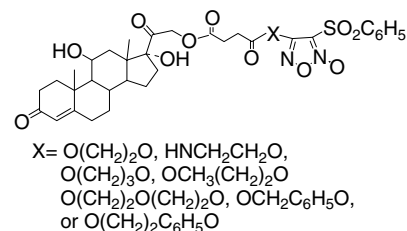
The indanylacetic acid structural motif has proven useful in the generation of potent and tunable PPAR ligands. Modification of the substituents on the linker and the heterocycle tail group modulated the selectivity at the different receptor subtypes.

**Design and synthesis of furoxan-based nitric oxide-releasing glucocorticoid derivatives with potent anti-inflammatory activity and improved safety**

pp 1062–1066

Lei Fang, Yihua Zhang,\* Jochen Lehmann,\* You Wang, Hui Ji and Dayong Ding

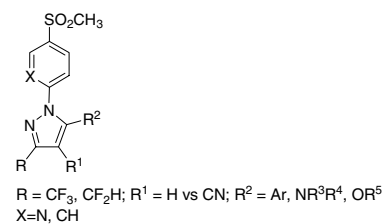
A series of furoxan-based nitric oxide-releasing glucocorticoid derivatives was synthesized and evaluated for their anti-inflammatory activity and safety.

**5-Heteroatom substituted pyrazoles as canine COX-2 inhibitors. Part III: Molecular modeling studies on binding contribution of 1-(5-methylsulfonyl)pyrid-2-yl and 4-nitrile**

pp 1067–1072

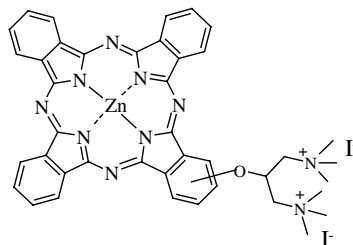
Subas M. Sakya,\* Xinjun Hou, Martha L. Minich, Bryson Rast, Andrei Shavnya, Kristin M. L. DeMello, Hengmiao Cheng, Jin Li, Burton H. Jaynes, Donald W. Mann, Carol F. Petras, Scott B. Seibel and Michelle L. Haven

The SAR of the 5-heteroatom and aryl substituted pyrazoles with 4-nitrile substitution shows substantial improvement in activity against the COX enzymes. Molecular modelling studies were done to understand the reasons for such difference in activity. The potential interactions of the nitrile and pyridyl nitrogen within the active site that could explain this difference are highlighted.

**Synthesis and in vitro photodynamic activity of mono-substituted amphiphilic zinc(II) phthalocyanines**

pp 1073–1077

Pui-Chi Lo, Baozhong Zhao, Wubiao Duan, Wing-Ping Fong, Wing-Hung Ko and Dennis K. P. Ng\*



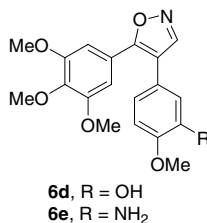
A novel series of mono-substituted zinc(II) phthalocyanines have been prepared which exhibit a high photodynamic activity against HT29 human colorectal carcinoma cells with IC<sub>50</sub> values down to 0.08  $\mu$ M.



**Synthesis and cytotoxic activities of 4,5-diarylisoxazoles**

pp 1078–1081

Chang-Ming Sun, Lee-Gin Lin, Hsi-Jung Yu, Chih-Yu Cheng, Ya-Chuan Tsai, Chi-Wei Chu, Yi-Hui Din, Yat-Pang Chau and Ming-Jaw Don\*



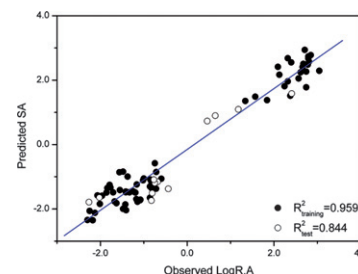
A series of 4,5-diarylisoxazoles related to combretastatin A-4 (**CA-4**) were synthesized, and compounds **6d** and **6e** showed strong cytotoxicity against three human cancer cell lines.

**Quantitative structure–activity relationship (QSAR) of tacrine derivatives against acetylcholinesterase (AChE) activity using variable selections**

pp 1082–1090

Mankil Jung,\* Jungae Tak, Yongnam Lee and Youngae Jung

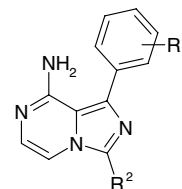
A diverse approach to the QSAR of tacrine derivatives against acetylcholinesterase (AChE) activity was studied using variable selections of stepwise multiple linear regression (MLR).

**1,3-Disubstituted-imidazo[1,5-a]pyrazines as insulin-like growth-factor-I receptor (IGF-IR) inhibitors**

pp 1091–1097

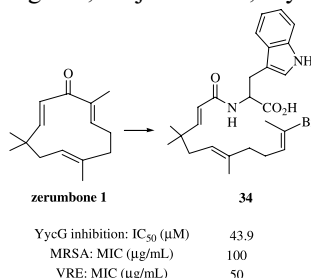
Mark J. Mulvihill,\* Qun-Sheng Ji, Doug Werner, Patricia Beck, Cara Cesario, Andrew Cooke, Matthew Cox, Andrew Crew, Hanqing Dong, Lixin Feng, K. W. Foreman, Gilda Mak, Anthony Nigro, Matthew O'Connor, Lydia Saroglou, Kathryn M. Stolz, Izabela Sujka, Brian Volk, Qinghua Weng and Robin Wilkes

A series of novel 8-amino-1,3-disubstituted-imidazo[1,5-a]pyrazines was designed and synthesized as IGF-IR inhibitors.

**Synthesis of a novel inhibitor against MRSA and VRE: Preparation from zerumbone ring opening material showing histidine-kinase inhibition**

pp 1098–1101

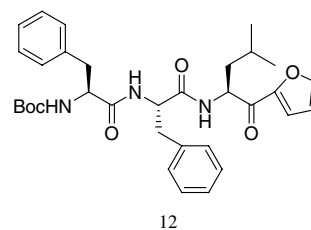
Takashi Kitayama,\* Risa Iwabuchi, Shu Minagawa, Seiji Sawada, Ryo Okumura, Kazuki Hoshino, John Cappiello and Ryutaro Utsumi\*



The synthesis of the novel YycG inhibitor **34** (IC<sub>50</sub> = 43.9 μM) showing growth inhibition against MRSA and VRE is reported.

**Design and synthesis of a novel class of furan-based molecules as potential 20S proteasome inhibitors** pp 1102–1106  
Yiqiu Fu, Bo Xu, Xiaomin Zou, Chao Ma, Xiaoming Yang, Ke Mou, Gang Fu, Yang Lü and Ping Xu\*

A novel class of furan-based compounds as potential 20S proteasome inhibitors have been designed and synthesized, among which nine compounds are peptide derivatives and six molecules are statine peptidomimetics. All the compounds were obtained steadily with moderate to high yield. Compound **12** was a selective moderate potent proteasome peptidomimetic inhibitor ( $IC_{50} = 7.85 \mu\text{M}$ , CT-L activity). It inhibited HepG2 and HL-60 proliferation effectively ( $IC_{50} = 34.2$  and  $37.07 \mu\text{M}$ , respectively).



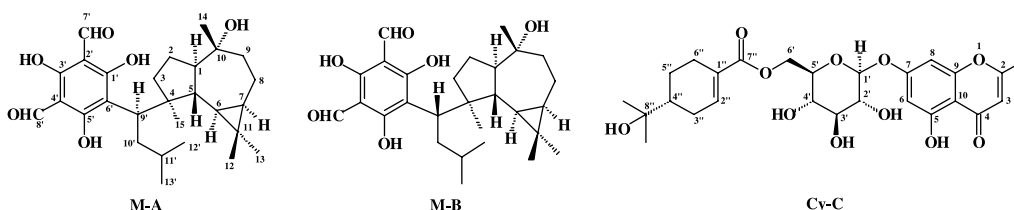
12



**Intestinal permeability of antiviral constituents from the fruits of *Eucalyptus globulus* Labill. in Caco-2 Cell Model**

pp 1107–1111

Xiu-wei Yang,\* Qing-mei Guo, Ying Wang, Wei Xu, Li Tian and Xiao-juan Tian



M-A

M-B

Cy-C

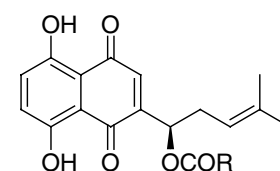
The intestinal absorption of M-A, M-B, and Cy-C was passive diffusion as the dominating process and Cy-C was partly ATP-dependent.

**Human ACAT inhibitory effects of shikonin derivatives from *Lithospermum erythrorhizon***

pp 1112–1116

Sojin An, Yong-Dae Park, Young-Ki Paik, Tae-Sook Jeong\* and Woo Song Lee\*

Among the tested shikonin derivatives (1–11), isobutanoyl-substituted analogue **2** preferentially inhibited hACAT-2 with an  $IC_{50}$  value of  $57.5 \mu\text{M}$ , and *n*-propanoyl- and 3-methylbutanoyl-substituted compounds **5** and **7** showed strong inhibitory activities in both hACAT-1 and -2. Furthermore, we demonstrated that compound **7** behaved as a potent ACAT inhibitor in not only in vitro assay system but also cell-based assay system.

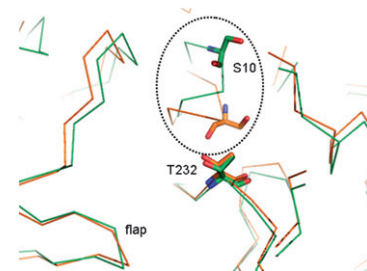


**$\beta$ -Secretase (BACE-1) inhibitors: Accounting for 10s loop flexibility using rigid active sites**

pp 1117–1121

Georgia B. McGaughey,\* Dennis Colussi, Samuel L. Graham, Ming-Tain Lai, Sanjeev K. Munshi, Philippe G. Nantermet, Beth Pietrak, Hemaka A. Rajapakse, Harold G. Selnick, Shaun R. Stauffer and M. Katharine Holloway

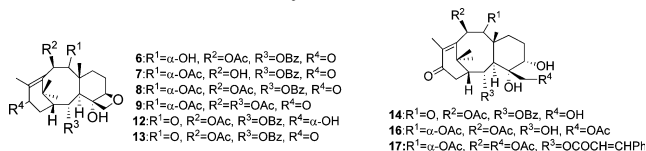
BACE-1 crystal structures demonstrating 10s loop motion were used to correlate  $K_i$  values from a series of tertiary carbinamine inhibitors with an empirical scoring function.



**Structure–activity relationships of some taxoids as multidrug resistance modulator**

pp 1122–1126

Toshiaki Hasegawa,\* Jao Bai, Shujun Zhang, Jinlan Wang, Junichi Matsubara, Junichi Kawakami, Akihiro Tomida, Takashi Tsuruo, Katsutoshi Hirose, Junichi Sakai, Midori Kikuchi, Mariko Abe and Masayoshi Ando\*



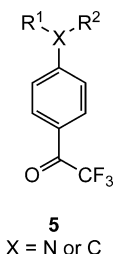
1,7-Deoxy-4-deacetylbaaccatin III (**12**), its five analogues **6–9**, **13**, and their oxetane ring opened derivatives **14**, **16**, and **17** showed significant activity as MDR reversal agent by the assay of the calcein accumulation toward MDR human ovarian cancer 2780AD cells. The most effective compound **12** in this assay is actually efficient for the recovery of cytotoxic activity of paclitaxel, adriamycin, and vincristine toward MDR 2780AD cells at the same level toward parental 2780 cells.

**Novel trifluoroacetophenone derivatives as malonyl-CoA decarboxylase inhibitors**

pp 1127–1130

David M. Wallace,\* Masayuki Haramura, Jie-Fei Cheng, Thomas Arrhenius and Alex M. Nadzan

A series of trifluoroacetophenone derivatives were prepared and evaluated as malonyl-CoA decarboxylase (MCD) inhibitors. Several of the ‘reverse amide’ analogs were found to be potent inhibitors of MCD enzyme activity. The trifluoroacetyl group may interact with the MCD active site as the hydrate, which can be stabilized with electron-withdrawing groups.

**OTHER CONTENTS**

Summary of instructions to authors

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\*Corresponding author

Supplementary data available via ScienceDirect

**COVER**

Typical snapshot of **7b** bound to HIV-RT from an MC simulation. Carbon atoms of **7b** are gold; from the left, Tyr181, Tyr188, Phe227, Leu100, Lys101; Trp229 at the top, Val106 at the bottom. H-bond with Lys101 O on right. Some residues in front including Glu138 have been removed for clarity. The water on N5 is also H-bonded to a carboxylate O of Glu138. [Thakur, V. T.; Kim, J. T.; Hamilton, A. D.; Bailey, C. M.; Domaal, R. A.; Wang, L.; Anderson, K. S.; Jorgensen, W. L. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5664.]

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