

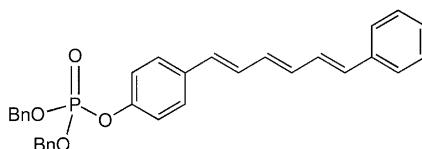
## Contents

### COMMUNICATIONS

#### Phosphorylated 1,6-diphenyl-1,3,5-hexatriene

pp 1075–1078

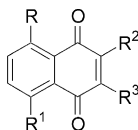
Ling Ma, Jessica C. Morgan, Wendy E. Stancill and William E. Allen\*



#### Design, synthesis and evaluation of novel 1,4-naphthoquinone derivatives as antifungal and anticancer agents

pp 1079–1083

Vishnu K. Tandon,\* Rakeshwar B. Chhor, Ravindra V. Singh, Sanjay Rai and Dharmendra B. Yadav

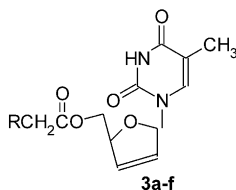


A series of 1,4-naphthoquinone derivatives were synthesized and found active against a number of fungal disease causative species and Walker 256 carcinoma cell lines.

#### Synthesis of stavudine amino acid ester prodrugs with broad-spectrum chemotherapeutic properties for the effective treatment of HIV/AIDS

pp 1085–1087

Dharmarajan Sriram,\* Perumal Yogeewari, Narasimharaghavan Srichakravarthy and Tanushree Ratan Bal

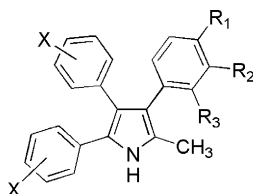


A series of amino acid ester prodrugs of stavudine were synthesized with ciprofloxacin, norfloxacin, isoniazide, pyrazinamide, piperazine and dimethylamino acetic acid in an effort to enhance spectrum of chemotherapeutic properties for the effective treatment of HIV/AIDS.

**Antihyperglycemic activity of 2-methyl-3,4,5-triaryl-1*H*-pyrroles in SLM and STZ models**

pp 1089–1092

Atul Goel,\* Nidhi Agarwal, Fateh V. Singh, Ashoke Sharon, Priti Tiwari, Manish Dixit, Ramendra Pratap, Arvind K. Srivastava, Prakas R. Maulik and Vishnu J. Ram\*



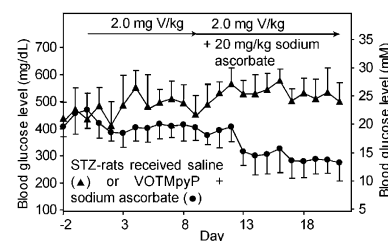
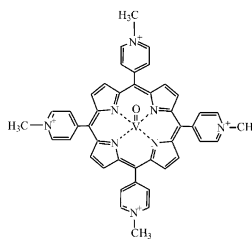
Synthesis and antihyperglycemic activity of various 2-methyl-3,4,5-triaryl-1*H*-pyrroles is described.

**A new candidate for insulinomimetic vanadium complex: synergism of oxovanadium(IV)porphyrin and sodium ascorbate**

pp 1093–1096

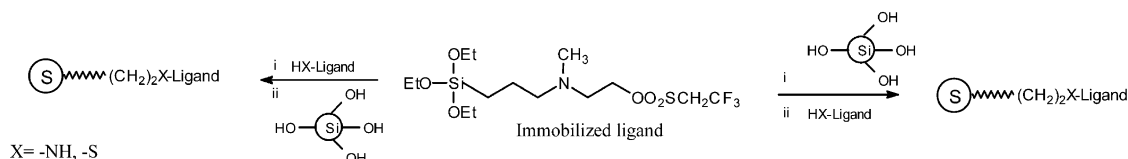
Hiromu Sakurai,\* Toshifumi Inohara, Yusuke Adachi, Kenji Kawabe, Hiroyuki Yasui and Jitsuya Takada

VOTMpyP with the VO(N<sub>4</sub>) coordination mode, was found to have a potent insulinomimetic activity on the basis of in vitro and in vivo experiments. When the complex was given simultaneously with sodium ascorbate, the high blood glucose levels of type 1 diabetic model STZ-rats were lowered by synergistic effect, probably sustaining the vanadyl state by means of ascorbate distributed in the organs and tissues of animals. This is the first finding on not only the insulinomimetic vanadyl–porphyrin complex but also the occurrence of a synergistic effect of VOTMpyP and sodium ascorbate to lower the high blood glucose levels in diabetic animals.

**A new heterobifunctional reagent for immobilization of biomolecules on glass surface**

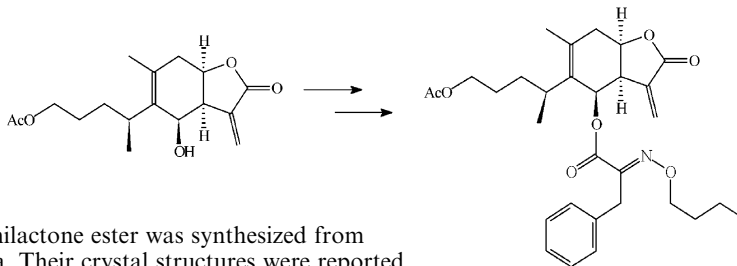
pp 1097–1099

P. Kumar, S. K. Agrawal, A. Misra and K. C. Gupta\*

**Studies on 1-*O*-acetylbritannilactone and its derivative, (2-*O*-butyloxime-3-phenyl)-propionyl-1-*O*-acetylbritannilactone ester**

pp 1101–1104

Shouxin Liu, Weiying Yan, Li Zhang, Naisheng Bai and Chi-Tang Ho\*

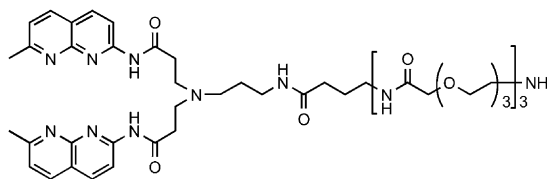


(2-*O*-butyloxime-3-phenyl) propionyl-1-*O*-acetylbritannilactone ester was synthesized from 1-*O*-acetylbritannilactone isolated from *Inula britannica*. Their crystal structures were reported. Both compounds inhibited the growth of human HL-60, Bel-7402 cell lines.

**Highly sensitive detection of GG mismatched DNA by surfaces immobilized naphthyridine dimer through poly(ethylene oxide) linkers**

pp 1105–1108

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

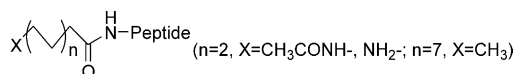


A 27-mer DNA duplex containing a G–G mismatch could be detected at 1 nM concentration by the surface where naphthyridine dimer was immobilized through three poly(ethylene oxide) linker units.

**Development of novel lipid–peptide hybrid compounds with antibacterial activity from natural cationic antibacterial peptides**

pp 1109–1113

Hyun-Sik Oh, Seunghee Kim, Hyeongjin Cho and Keun-Hyeung Lee\*

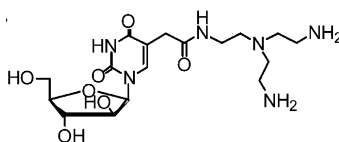


We designed and synthesized novel lipid–peptide hybrid compounds with antibacterial activity and characterized the important structural parameters for the activity.

**Synthesis and antisense properties of oligodeoxyribonucleotides containing C5-substituted arabinofuranosyluracil**

pp 1115–1118

Hiroaki Ozaki,\* Kiyohiro Nakajima, Masayasu Kuwahara and Hiroaki Sawai

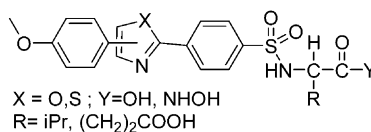


An oligodeoxyribonucleotide (ODN) containing three C5-substituted arabinofuranosyluracils was synthesized by the post-synthetic modification method. The modified ODN could induce RNase H activity and was resistant against nuclease.

**New heteroarylbenzenesulphonamides as matrix metalloproteinase inhibitors**

pp 1119–1121

Frédéric Delbecq, Guy Cordonnier, Nicole Pommery, Didier Barbry\* and Jean-Pierre Hénichart

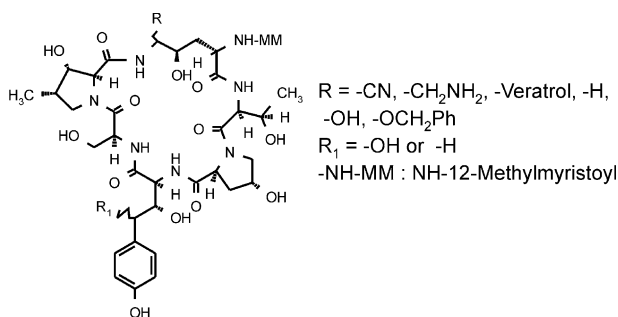


The synthesis and evaluation of thiazolyl- and oxazolylbenzenesulphonamides are described.

**Approaches towards the stabilization of hemiaminal function at ornithine unit of mulundocandin**

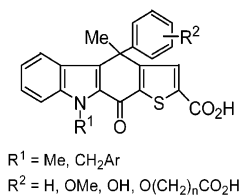
pp 1123–1128

Bansi Lal\* and Vitthal Genbhau Gund

**Carbazolothiophene-2-carboxylic acid derivatives as endothelin receptor antagonists**

pp 1129–1132

Govindarajulu Babu, Hui-Ming Yu, Shyh-Ming Yang and Jim-Min Fang\*

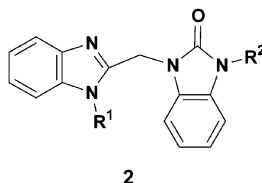


The carbazolothiophene compounds show inhibition against the endothelin-1 induced increase of intracellular calcium ion concentration.

**Respiratory syncytial virus inhibitors. Part 2: Benzimidazol-2-one derivatives**

pp 1133–1137

Kuo-Long Yu, Yi Zhang, Rita L. Civiello, Ashok K. Trehan, Bradley C. Pearce, Zhiwei Yin, Keith D. Combrink, H. Belgin Gulgeze, Xiangdong Alan Wang, Kathleen F. Kadow, Christopher W. Cianci, Mark Krystal and Nicholas A. Meanwell\*

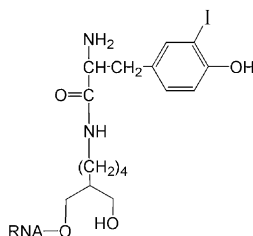


Structure–activity relationships for a series of benzimidazol-2-one-based inhibitors of respiratory syncytial virus are described. These studies focused on structural variation of the benzimidazol-2-one substituent, a vector inaccessible in a series of benzotriazole derivatives on which **2** is based, and revealed a broad tolerance for substituent size and functionality.

**Biodistribution of phosphodiester and phosphorothioate siRNA**

pp 1139–1143

Dwaine A. Braasch, Zain Paroo, Anca Constantinescu, Gang Ren, Orhan K. Öz, Ralph P. Mason and David R. Corey\*

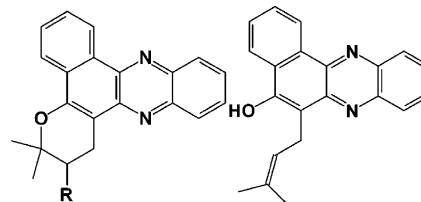


**Antimalarial activity of phenazines from lapachol,  $\beta$ -lapachone and its derivatives against *Plasmodium falciparum* in vitro and *Plasmodium berghei* in vivo**

pp 1145–1149

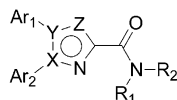
Valter F. de Andrade-Neto, Marília O. F. Goulart, Jorge F. da Silva Filho, Matuzalém J. da Silva, Maria do Carmo F. R. Pinto, Antônio V. Pinto, Mariano G. Zalis, Luzia H. Carvalho and Antoniana U. Krettli\*

Benzo[*a*]phenazines derived from 1,2-naphthoquinone, lapachol,  $\beta$ -lapachone and some derivatives were assayed in vitro against *Plasmodium falciparum* (strains BH3 and clones HB3, D6 and W2) and in vivo against *P. berghei* in mice. The phenazines containing polar (–Br, –I) and ionizable (–SO<sub>3</sub>H, –OH) groups had the highest in vitro antimalarial activities (IC<sub>50</sub> from 1.90 to 9.44  $\mu$ M); the 3-sulfonide (R = SO<sub>3</sub>H) was active in vivo, providing, possibly, leads for development of new antimalarial drugs.

**Potent imidazole and triazole CB<sub>1</sub> receptor antagonists related to SR141716**

pp 1151–1154

Brian Dyck,\* Val S. Goodfellow, Teresa Phillips, Jonathan Grey, Mustapha Haddach, Martin Rowbottom, Gregory S. Naeve, Brock Brown and John Saunders

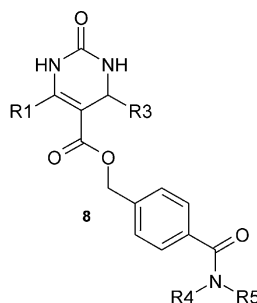


Diaryl-substituted pyrazole-, imidazole- and triazole-based carboxamides were synthesized and their affinity for human CB<sub>1</sub> receptor determined.

**Discovery of a dihydropyrimidine series of molecules that selectively mimic the biological actions of calcitonin**

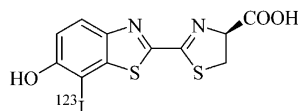
pp 1155–1159

Jay M. Matthews,\* Fina Liotta, William Hageman, Ralph A. Rivero, Lori Westover, Maria Yang, Jun Xu and Keith Demarest

**Synthesis of 7'-[<sup>123</sup>I]iodo-D-luciferin for in vivo studies of firefly luciferase gene expression**

pp 1161–1163

Sang-Yoon Lee, Yearn Seong Choe,\* Kyung-Han Lee, Jeewoo Lee, Yong Choi and Byung-Tae Kim

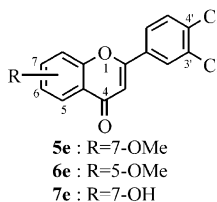


Synthesis of 7'-[<sup>123</sup>I]/<sup>127</sup>I]iodo-D-luciferin and its binding property to firefly luciferase are described.

**Synthesis and inhibitory activity against COX-2 catalyzed prostaglandin production of chrysin derivatives**

pp 1165–1167

Tran Thanh Dao, Yeon Sook Chi, Jeongsoo Kim, Hyun Pyo Kim, Sanghee Kim and Haeil Park\*

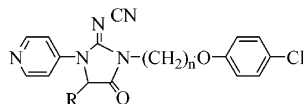


A series of chrysin derivatives were prepared from 2,4-, 2,6-dihydroxyacetophenones and 2-hydroxyacetophenone in 2 to 4 steps, respectively. The inhibitory activities of chrysin derivatives were determined by measuring prostaglandin production of RAW 264.7 cells treated with lipopolysaccharide. We found that chrysin derivatives with 3',4'-dichloro substituents (**5e**, **6e** and **7e**) exhibited the strongest activity among them.

**Synthesis and in vitro cytotoxicity of 5-substituted 2-cyanoimino-4-imidazodinone and 2-cyanoimino-4-pyrimidinone derivatives**

pp 1169–1172

Jyh-Haur Chern,\* Kak-Shan Shia, Chung-Ming Chang, Chung-Chi Lee, Yen-Chun Lee, Chia-Liang Tai, Ying-Ting Lin, Chih-Shiang Chang and Huan-Yi Tseng

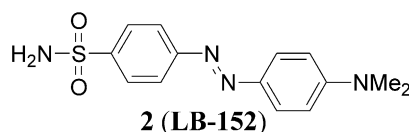


A series of 5-substituted 2-cyanoimino-4-imidazodinone and 2-cyanoimino-4-pyrimidinone derivatives were synthesized and their anticancer cytotoxicity was evaluated in in vitro assay. One of the derivatives, compound **11** exhibited the most potent activity with IC<sub>50</sub> in the nanomolar range.

**Aβ Aggregation inhibitors. Part 1: Synthesis and biological activity of phenylazo benzenesulfonamides**

pp 1173–1176

Shwu-Jiuan Lin, Young-Ji Shiao, Chih-Wen Chi and Li-Ming Yang\*

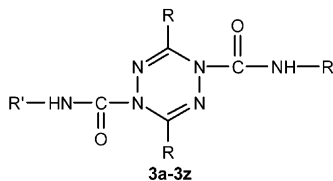


Phenylazo benzenesulfonamide **2 (LB-152)** was synthesized and evaluated for inhibition of Aβ<sub>40</sub> aggregation and neurotoxicity.

**Synthesis and antitumor activity of s-tetrazine derivatives**

pp 1177–1181

Wei-Xiao Hu,\* Guo-Wu Rao and Ya-Quan Sun

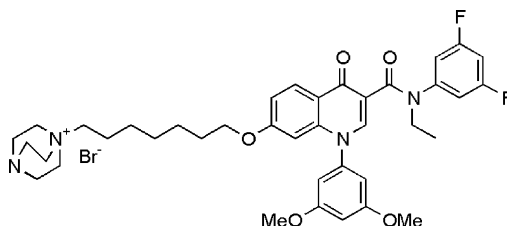


Fifty-five compounds were prepared by the new reactions and their structures were determined by X-ray analysis. Their antitumor activities in vitro were evaluated. The results show s-tetrazine derivative especially 1,4-dihydro-s-tetrazine is a kind of compound which possesses potential antitumor activities and that warrants further investigation.

### A novel class of apical sodium-dependent bile acid transporter inhibitors: the amphiphilic 4-oxo-1-phenyl-1,4-dihydroquinoline derivatives

pp 1183–1186

Hitoshi Kurata,\* Sayaka Suzuki, Yasuo Ohhata, Takuya Ikeda, Toru Hasegawa, Ken Kitayama, Toshimori Inaba, Keita Kono and Takafumi Kohama

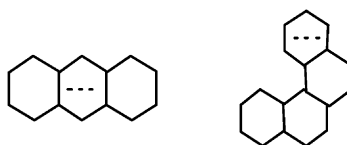


The synthesis, ASBT inhibition and serum cholesterol lowering effect of novel 4-oxo-1-phenyl-1,4-dihydroquinoline derivatives are reported.

### Correlations between the benzene character of acenes or helicenes and simple molecular descriptors

pp 1187–1191

Padmakar V. Khadikar,\* Sheela Joshi, Amrit V. Bajaj and Dheeraj Mandloi

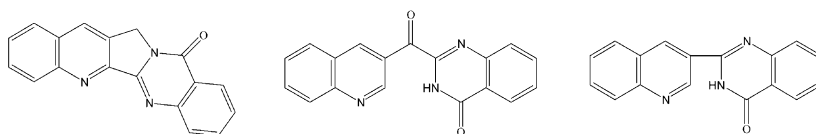


Aromatic stabilities of acenes and helicenes, which are responsible for their biological, environmental and cancerous behavior have been modeled using a newly introduced Sadhana (Sd) and A indices. The results are compared with those obtained from PI (Padmakar-Ivan) index. The regression analysis has shown that excellent results are obtained by considering acenes and helicenes as separate classes of isomeric benzenoid hydrocarbons. Also that out of the three indices used (A, Sd, PI), the A index gave better results.

### Novel quinazoline–quinoline alkaloids with cytotoxic and DNA topoisomerase II inhibitory activities

pp 1193–1196

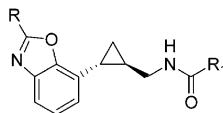
Zhongze Ma,\* Yoshio Hano, Taro Nomura and Yingjie Chen



### Design and synthesis of benzoxazole derivatives as novel melatoninerigic ligands

pp 1197–1200

Li-Qiang Sun,\* Jie Chen, Katherine Takaki, Graham Johnson, Lawrence Iben, Cathy D. Mahle, Elaine Ryan and Cen Xu

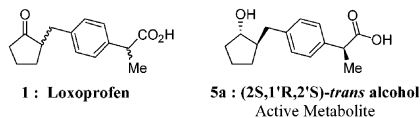


A novel series of benzoxazole derivatives was synthesized and evaluated as melatoninerigic ligands. The binding affinity of these compounds for human MT<sub>1</sub> and MT<sub>2</sub> receptors was determined using 2-[<sup>125</sup>I]-iodomelatonin as the radioligand. The results of the SAR studies in this series led to the identification of compound **28**, which exhibited better MT<sub>1</sub> and MT<sub>2</sub> receptor affinities than melatonin itself. This work also established the benzoxazole nucleus as a melatoninerigic pharmacophore, which served as an isosteric replacement to the previously established alkoxyaryl core.

**Evaluation of loxoprofen and its alcohol metabolites for potency and selectivity of inhibition of cyclooxygenase-2**

pp 1201–1203

Denis Riendeau,\* Myriam Salem, Angela Styhler, Marc Ouellet,  
Joseph A. Mancini and Chun Sing Li

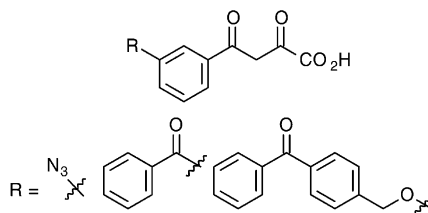


The four *trans*-alcohol metabolites and a mixture of the *cis*-alcohol metabolites of loxoprofen were evaluated for potency and selectivity of inhibition of COX-2 over COX-1. The (2*S*,1'*R*,2'*S*)-*trans*-alcohol metabolite was found to be the most potent inhibitor of COX-2 and to cause a nonselective inhibition of COX-2 and COX-1 in both enzyme and human whole blood assays.

**Design and synthesis of photoactivatable aryl diketo acid-containing HIV-1 integrase inhibitors as potential affinity probes**

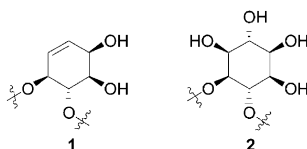
pp 1205–1207

Xuechun Zhang, Christophe Marchand, Yves Pommier and Terrence R. Burke, Jr.\*

**New oligomers of conduritol-F and *muco*-inositol. Synthesis and biological evaluation as glycosidase inhibitors**

pp 1209–1212

Stanley Freeman and Tomas Hudlicky\*

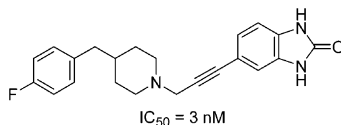


The synthesis, structure, and biological evaluation of oligomers whose structural motifs are based on conduritol-F (**1**) and *muco*-inositol (**2**) are reported.

**Subtype selective NMDA receptor antagonists: evaluation of some novel alkynyl analogues**

pp 1213–1216

Brian E. Kornberg,\* Sham S. Nikam, Jon L. Wright, Suzanne R. Kesten, Leonard T. Meltzer,  
Linda Coughenour, Bridget Barr, Kevin A. Serpa and Julie McCormick



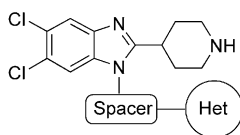
The synthesis and SAR of a variety of benzylpiperidinyl-acetylenes with NR2B receptor selectivity is described.



**Synthesis and biological evaluations of novel benzimidazoles as potential antibacterial agents**

pp 1217–1220

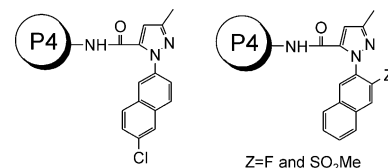
Yun He,\* Jun Yang, Baogen Wu, Lisa Risen and Eric E. Swayze

**1-(2-Naphthyl)-1H-pyrazole-5-carboxylamides as potent factor Xa inhibitors. Part 2: A survey of P4 motifs**

pp 1221–1227

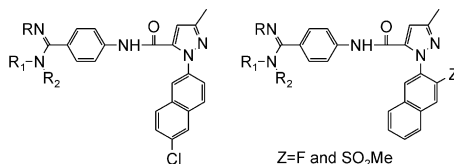
Zhaozhong J. Jia,\* Yanhong Wu, Wenrong Huang, Penglie Zhang, Lane A. Clizbe, Erick A. Goldman, Uma Sinha, Ann E. Arfsten, Susan T. Edwards, Merlyn Alphonso, Athiwat Hutchaleelaha, Robert M. Scarborough and Bing-Yan Zhu\*

A variety of P4 motifs have been examined for optimization of the 1-(2-naphthyl)-1H-pyrazole-5-carboxylamide-based factor Xa inhibitors. Highly potent factor Xa inhibitors with desired in vitro anticoagulant activity and excellent oral PK profiles have been discovered.

**1-(2-Naphthyl)-1H-pyrazole-5-carboxylamides as potent factor Xa inhibitors. Part 3: Design, synthesis and SAR of orally bioavailable benzamidine-P4 inhibitors**

pp 1229–1234

Zhaozhong J. Jia,\* Yanhong Wu, Wenrong Huang, Penglie Zhang, Yonghong Song, John Woolfrey, Uma Sinha, Ann E. Arfsten, Susan T. Edwards, Athiwat Hutchaleelaha, Stanley J. Hollennbach, Joseph L. Lambing, Robert M. Scarborough and Bing-Yan Zhu\*

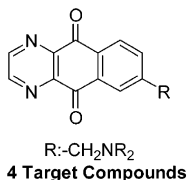


Using *N,N*-dialkylated benzamidines as the novel P4 motifs, highly potent and selective factor Xa inhibitors with desired in vitro anticoagulant activity, excellent oral bioavailability and long half-life have been discovered.

**Synthesis and in vitro evaluation of 7-dialkylaminomethylbenzo[g]quinoxaline-5,10-diones**

pp 1235–1237

Heesoon Lee,\* Sungmoon Cho, Kwon Namgoong, Jae-Kyung Jung, Jungsook Cho and Sung-Il Yang

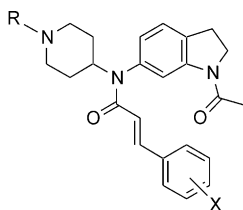


A series of benzo[g]quinoxaline-5,10-dione derivatives carrying a 7-dialkylaminomethyl substituent was synthesized and their in vitro cytotoxic activities were evaluated against four human cancer cell lines (HCT-15, SK-OV-3, MD-MB-468 and T-47D). The most active compound **9d** showed cytotoxic activity comparable to that of doxorubicin against HCT-15 cancer cell line.

**Novel non-peptidic neuropeptide Y Y<sub>2</sub> receptor antagonists**

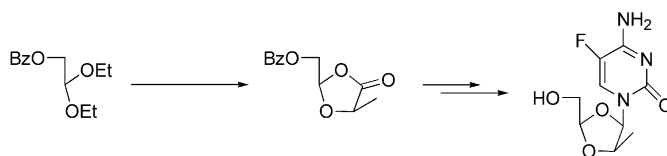
pp 1239–1242

Jill A. Jablonowski,\* Wenying Chai, Xiaobing Li, Dale A. Rudolph, William V. Murray, Mark A. Youngman, Scott L. Dax, Diane Nepomuceno, Pascal Bonaventure, Timothy W. Lovenberg and Nicholas I. Carruthers

**Synthesis of 5'-C-methyl-1',3'-dioxolan-4'-yl nucleosides**

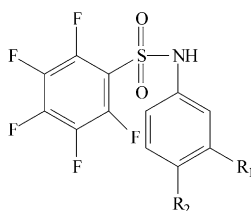
pp 1243–1245

Jinfa Du,\* Steven Patterson, Junxing Shi, Byoung-Kwon Chun, Lieven J. Stuyver and Kyoichi A. Watanabe

**Synthesis, biodistribution and micro-PET imaging of radiolabeled antimitotic agent T138067 analogues**

pp 1247–1251

Xiangshu Fei, Qi-Huang Zheng,\* Ji-Quan Wang, K. Lee Stone, Tanya D. Martinez, Kathy D. Miller, George W. Sledge and Gary D. Hutchins



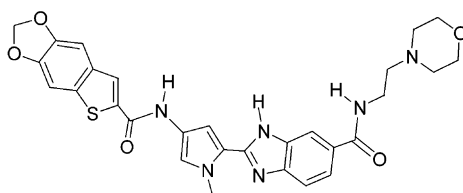
T138067, R<sub>1</sub>=F; R<sub>2</sub>=OCH<sub>3</sub>  
<sup>11</sup>C]T138067, R<sub>1</sub>=F; R<sub>2</sub>=O<sup>11</sup>CH<sub>3</sub>  
<sup>18</sup>F]T138067, R<sub>1</sub>=<sup>18</sup>F; R<sub>2</sub>=OCH<sub>3</sub>

**DNA binding ligands targeting drug-resistant Gram-positive bacteria.**

pp 1253–1257

**Part 1: Internal benzimidazole derivatives**

Roland W. Bürli, Dustin McMinn, Jacob A. Kaizerman, Wenhao Hu, Yigong Ge, Quinn Pack, Vernon Jiang, Matthew Gross, Martin Garcia, Richard Tanaka and Heinz E. Moser\*



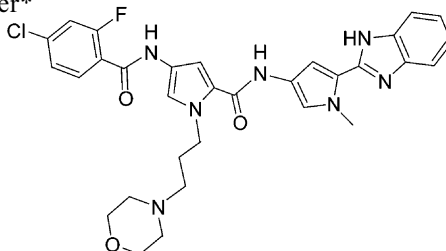
Novel DNA minor-groove binding ligands with a promising antibacterial profile are described. Apart from excellent in vitro potency against multiple Gram-positive bacteria including drug-resistant strains, a small subset of compounds was active against Gram-negative bacteria.

**DNA binding ligands targeting drug-resistant Gram-positive bacteria.**

pp 1259–1263

**Part 2: C-terminal benzimidazoles and derivatives**

Roland W. Bürli, Peter Jones, Dustin McMin, Quan Le, Jian-Xin Duan, Jacob A. Kaizerman, Stacey Difuntorum and Heinz E. Moser\*

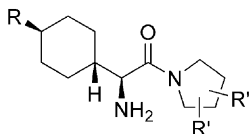


The synthesis and in vitro potency of DNA minor-groove binding antibacterials lacking the C-terminal amide bond are described focusing on variations of the N-terminal unit, the internal amino group, and the C-terminal ring system.

**Fluoropyrrolidine amides as dipeptidyl peptidase IV inhibitors**

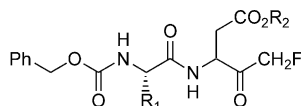
pp 1265–1268

Charles G. Caldwell,\* Ping Chen, Jiafang He, Emma R. Parmee, Barbara Leiting, Frank Marsilio, Reshma A. Patel, Joseph K. Wu, George J. Eiermann, Aleksandr Petrov, Huaibing He, Kathryn A. Lyons, Nancy A. Thornberry and Ann E. Weber

**Dipeptidyl aspartyl fluoromethylketones as potent caspase-3 inhibitors: SAR of the P<sub>2</sub> amino acid**

pp 1269–1272

Yan Wang, Jin-Chen Huang, Zhang-lin Zhou, Wu Yang, John Guastella, John Drewe and Sui Xiong Cai\*

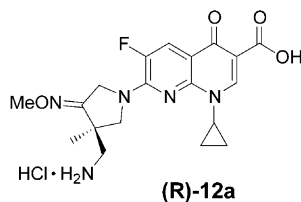


The synthesis and SAR of dipeptidyl aspartyl fluoromethylketones as caspase-3 inhibitors is reported.

**Syntheses and biological evaluation of new fluoroquinolone antibacterials containing chiral oximinopyrrolidine**

pp 1273–1277

Dong Rack Choi,\* Jung Han Shin, Jin Yang, Sue Hye Yoon and Yong Ho Jung

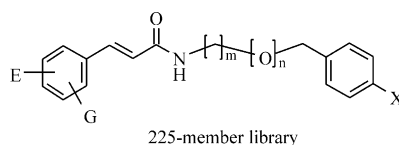


The design and syntheses of new fluoroquinolone antibacterial agents, (R)-12a and (R)-12e are described. Both have excellent in vitro antibacterial activities and pharmacokinetic profiles.

**Solid-phase synthesis of an *N*-(phenylalkyl)cinnamide library via Horner–Wadsworth–Emmons reaction**

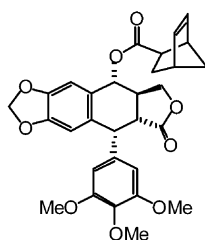
pp 1279–1281

Csaba Wéber,\* Attila Bielik, Györgyi I. Szendrei, György M. Keserű and István Greiner

E, G = H, OH, alkyl., alkoxy, NO<sub>2</sub>, CN, etc.; X = H, Cl, Br; *m* = 1, 2, 3, *n* = 0, 1.**Synthesis and cytotoxicity of hydrophobic esters of podophyllotoxins**

pp 1283–1286

J. L. López-Pérez,\* E. del Olmo, B. de Pascual-Teresa, A. Abad and A. San Feliciano

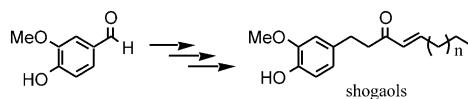


Diverse norbornenecarboxylate esters of podophyllotoxin and diastereoisomers have been prepared through Diels–Alder cycloaddition, by treating their dienophilic acrylates with cyclopentadiene, some of them showing IC<sub>50</sub> values about 4 nM, that represented an improvement in potency with respect to the natural reference drug.

**Side-chain length is important for shogaols in protecting neuronal cells from β-amyloid insult**

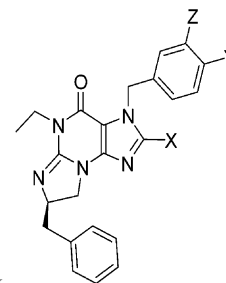
pp 1287–1289

Darrick S. H. L. Kim\* and Jin Yung Kim

**SAR development of polycyclic guanine derivatives targeted to the discovery of a selective PDE5 inhibitor for treatment of erectile dysfunction**

pp 1291–1294

Dmitri A. Pissarnitski,\* Theodros Asberom, Craig D. Boyle, Samuel Chackalamannil, Madhu Chintala, John W. Clader, William J. Greenlee, Yueqing Hu, Stanley Kurowski, Joyce Myers, Jairam Palamanda, Andrew W. Stamford, Subbarao Vemulapalli, Yuguang Wang, Peng Wang, Ping Wu and Ruo Xu

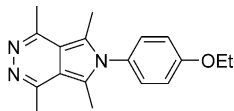


A potent and selective series of phosphodiesterase 5 inhibitors was discovered (PDE5 IC<sub>50</sub> = 1.3–11.0 nM, PDE6/5 = 116–600).

**Synthesis and biological evaluation of 6-aryl-6*H*-pyrrolo[3,4-*d*]pyridazine derivatives: high-affinity ligands to the  $\alpha_2\delta$  subunit of voltage gated calcium channels**

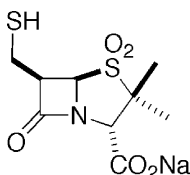
pp 1295–1298

Brian A. Stearns,\* Naomi Anker, Jeannie M. Arruda, Brian T. Campbell, Chixu Chen, Meryll Cramer, Tao Hu, Xiaohui Jiang, Kenneth Park, Kun Kun Ren, Marciano Sablad, Angelina Santini, Herve Schaffhauser, Mark O. Urban and Benito Munoz

**Penicillin-derived inhibitors that simultaneously target both metallo- and serine- $\beta$ -lactamases**

pp 1299–1304

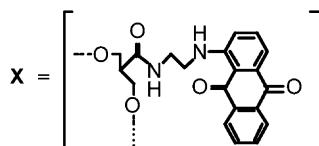
John D. Buynak,\* Hansong Chen, Lakshminaryana Vogeti, Venkat Rao Gadachanda, Christine A. Buchanan, Timothy Palzkill, Robert W. Shaw, James Spencer and Timothy R. Walsh

**Novel anthraquinone conjugate of 2,2-bis(hydroxymethyl)propionic acid incorporated to a TFO with phosphodiester linkage facilitates triplex formation with dsDNA bearing a pyrimidine-gapped polypurine sequence**

pp 1305–1308

Megumi Sato, Tomohisa Moriguchi and Kazuo Shinozuka\*

3' -TCTTTTTTTTCTT**X**C-5' **GK-302**

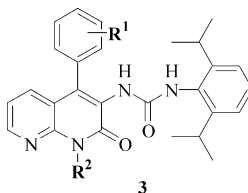


Novel TFO bearing an intercalator forms a stable triplex with a purimidine-gapped polypurine of dsDNA.

**Synthesis and structure–activity relationship studies on a novel series of naphthylidinoylureas as inhibitors of acyl-CoA:cholesterol *O*-acyltransferase (ACAT)**

pp 1309–1311

Satoshi Ohnuma,\* Masami Muraoka, Katsuhisa Ioriya and Naohito Ohashi

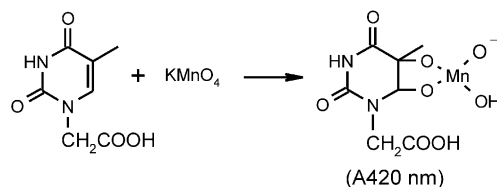


The synthesis and structure–activity relationships of *N*-phenyl-*N'*-[3-(4-phenylnaphthylidinoyl)]urea derivatives **3** as a novel structural class of potent ACAT inhibitors are described.

**UV–visible spectral identification of the solution-phase and solid-phase permanganate oxidation reactions of thymine acetic acid**

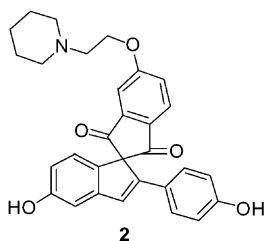
pp 1313–1315

Chinh T. Bui,\* Lien A. Sam and Richard G. H. Cotton

**Comparison of 2-phenylspiroindenes and 2-phenylspiroindenediones as estrogen receptor ligands—modeling and binding data don't agree!**

pp 1317–1321

Timothy A. Blizzard,\* Ralph T. Mosley, Elizabeth T. Birzin, Wanda Chan and Milton L. Hammond

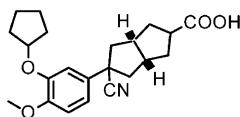


A series of 2-phenylspiroindenediones (e.g., **2**) was prepared. The spiroindenediones were found to be less active than the corresponding spiroindenes as estrogen receptor ligands and failed to demonstrate the receptor subtype selectivity that molecular modeling predicted.

**Orally active PDE4 inhibitors with therapeutic potential**

pp 1323–1327

Hiroshi Ochiai, Tazumi Ohtani, Akiharu Ishida, Katuya Kishikawa, Takaaki Obata, Hisao Nakai\* and Masaaki Toda

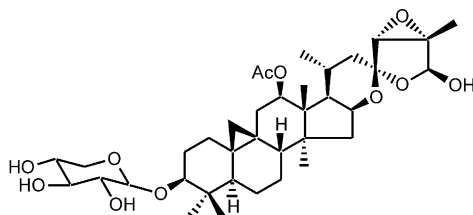


Optimization of the spatial arrangement of the three pharmacophores is attempted using a bicyclo[3.3.0]octane template. Synthesis and biological evaluation is reported.

**Anti-AIDS Agents. Part 57: Actein, an anti-HIV principle from the rhizome of *Cimicifuga racemosa* (black cohosh), and the anti-HIV activity of related saponins**

pp 1329–1332

Nobuko Sakurai, Jiu-Hong Wu, Yutaka Sashida, Yoshihiro Mimaki, Tamotsu Nikaido, Kazuo Koike, Hideji Itokawa and Kuo-Hsiung Lee\*

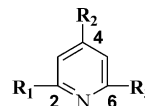
**1** Actein (26S:26R = 3:1)

**Synthesis, topoisomerase I inhibition and structure–activity relationship study of 2,4,6-trisubstituted pyridine derivatives**

pp 1333–1337

Long-Xuan Zhao, Yoon-Soo Moon, Arjun Basnet, Eun-kyung Kim, Yurngdong Jahng,\* Jae Gyu Park, Tae Cheon Jeong, Won-Jea Cho, Sang-Un Choi, Chong Ock Lee, Sun-Young Lee, Chong-Soon Lee and Eung-Seok Lee\*

For the development of new anticancer agents, phenyl, 2-pyridyl, 2-furyl, 2-thienyl, 2-furylvinyl and 2-thienylvinyl substituted derivatives on 2,4,6-position in pyridine moiety were prepared and evaluated for their topoisomerase I inhibitory activity. Among the thirteen prepared compounds, four compounds exhibited strong topoisomerase I inhibitory activity. A structure–activity relationship study indicated that the 2-thienyl-4-furylpyridine skeleton was important for topoisomerase I inhibitory activity.

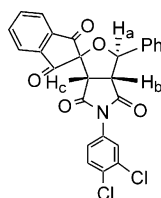


**R**<sub>1</sub>, **R**<sub>2</sub>, **R**<sub>3</sub>: H, phenyl, 2-pyridyl, 2-furyl, 2-thienyl, 2-furylvinyl, 2-thienylvinyl

**A series of spirocyclic analogues as potent inhibitors of bacterial phenylalanyl-*t*RNA synthetases**

pp 1339–1342

Xiang Y. Yu,\* John Finn, Jason M. Hill, Zhong G. Wang, Dennis Keith, Jared Silverman and N. Oliver



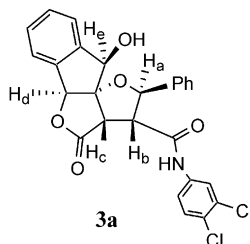
**1b** (*trans*)

We have identified a series of spirocyclic furan and pyrrolidine inhibitors of *E. faecalis* and *S. aureus* phenylalanyl-*t*RNA synthetases. The most potent analogue **1b** showed IC<sub>50</sub> = 5 nM (*E. faecalis* PheRS) and IC<sub>50</sub> = 2 nM (*S. aureus* PheRS) with high selectivity over the human enzyme. The crystal X-ray structure of analogue **1b** was determined.

**A series of heterocyclic inhibitors of phenylalanyl-*t*RNA synthetases with antibacterial activity**

pp 1343–1346

Xiang Y. Yu,\* John Finn, Jason M. Hill, Zhong G. Wang, Dennis Keith, Jared Silverman and N. Oliver



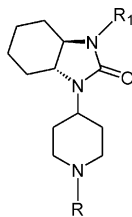
**3a**

A series of novel heterocyclic analogues have been synthesized and evaluated for their ability to inhibit phenylalanyl-*t*RNA synthetases and act as antibacterial agents. Several analogues have good antibacterial activity against *Staphylococcus aureus*. Minimum inhibitory concentration (MIC) for analogue **3a** was 3.1 µg/mL against *S. aureus*.

**Design and synthesis of novel small molecule N/OFQ receptor antagonists**

pp 1347–1351

Zhengming Chen,\* R. Richard Goehring, Kenneth J. Valenzano and Donald J. Kyle



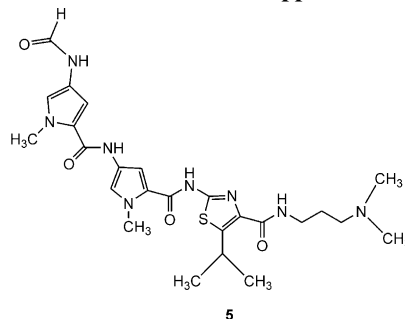
Small molecule N/OFQ receptor antagonists were designed and synthesized to further investigate the therapeutic potential of N/OFQ receptor modulators. The resulting octahydrobenzimidazol-2-ones **14** and **23** show excellent antagonistic activity towards both N/OFQ and mu receptors with high affinity to the human N/OFQ receptor.

**DNA binding of a short lexitropsin**

pp 1353–1356

Nahoum G. Anthony, Keith R. Fox, Blair F. Johnston, Abedawn I. Khalaf, Simon P. Mackay, Iain S. McGroarty, John A. Parkinson, Graham G. Skellern, Colin J. Suckling\* and Roger D. Waigh

Footprinting, capillary electrophoresis, molecular modelling and NMR studies have been used to examine the binding of **5** to DNA. This molecule, which contains an isopropyl-substituted thiazole in place of one of the *N*-methylpyrroles, is selective for the sequence 5'-ACTAGT-3' to which it binds with high affinity. Two molecules bind side-by-side in the minor groove, but their binding is staggered so that the molecule reads six base pairs, unlike the related natural products, which tend to bind to four-base-pair sequences. The result suggests that high affinity and selectivity may be gained without resort to very large molecules, which may be difficult to deliver to the site of action.

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**Instructions to contributors**

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\*Corresponding author

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

**COVER**

Cover figure provided by **Indraneel Ghosh**, Department of Chemistry, University of Arizona. The cover depicts the **Dual Surface Selection** methodology developed by the author: the blue helix of htB1 (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htB1 (center) allows for functional selection against thrombin (right). © 2003 Indraneel Ghosh. Published by Elsevier Ltd.



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