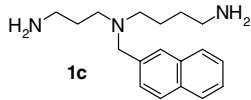
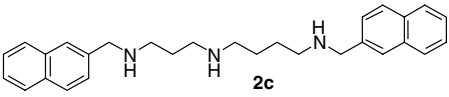


Contents

ARTICLES

**Polyamines and the NMDA receptor: Modifying intrinsic activities with aromatic substituents** pp 2837–2841

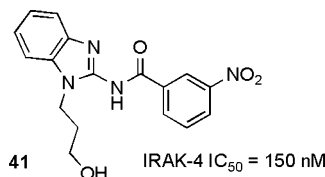
Michael L. Berger,\* Abdallah Y. Bitar, Matthew J. Waitner, Patrick Rebernik and Mary C. O'Sullivan

	IC <sub>50</sub> (μM)	attenuation by 30 μM SPM
 <p><b>1c</b></p>	9.8	13.1
 <p><b>2c</b></p>	4.4	2.1

The inhibiting effects of 34 spermidine and spermine derivatives on the binding of [<sup>3</sup>H]MK-801 to NMDA receptors on rat brain membranes were investigated. Several compounds, including **1c**, appeared to inhibit radioligand binding via the polyamine regulatory site, whereas others, including **2c**, more likely acted directly at the channel.

**Discovery and initial SAR of inhibitors of interleukin-1 receptor-associated kinase-4** pp 2842–2845

Jay P. Powers,\* Shyun Li, Juan C. Jaen, Jinqian Liu, Nigel P. C. Walker, Zhulun Wang and Holger Wesche



High-throughput screening of a small-molecule compound library resulted in the identification of a novel series of *N*-acyl 2-aminobenzimidazoles that are potent inhibitors of interleukin-1 receptor-associated kinase-4.

**Rediscovery of natural products using genomic tools** pp 2846–2849

Akira Kawamura,\* Angelika Brekman, Yevgeniy Grigoryev, Tal H. Hasson, Anna Takaoka, Stephanie Wolfe and Clifford E. Soll



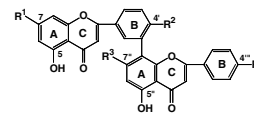
A new screening methodology was developed to uncover natural products that can regulate cellular transcription.



**Osteoblast differentiation stimulating activity of biflavonoids from *Cephalotaxus koreana***

pp 2850–2854

Mi Kyeong Lee, Song Won Lim, Hyekyung Yang, Sang Hyun Sung, Heum-Sook Lee, Mi Jung Park and Young Choong Kim\*

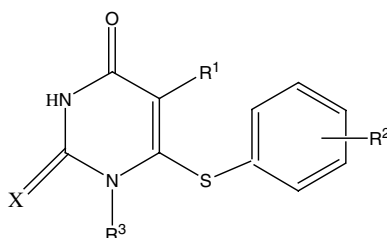
Bilobetin (1), sciadopitysin (5), and 7,4',7'',4-O-methyl-amentoflavone (6), biflavonoids isolated from *Cephalotaxus koreana* increased osteoblast differentiation.

Comps	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>
1	OH	OCH <sub>3</sub>	OH	OH
2	OCH <sub>3</sub>	OCH <sub>3</sub>	OH	OH
3	OH	OCH <sub>3</sub>	OCH <sub>3</sub>	OH
4	OCH <sub>3</sub>	OCH <sub>3</sub>	OCH <sub>3</sub>	OH
5	OCH <sub>3</sub>	OCH <sub>3</sub>	OH	OCH <sub>3</sub>
6	OCH <sub>3</sub>	OCH <sub>3</sub>	OCH <sub>3</sub>	OCH <sub>3</sub>

**Quantitative structure–activity relationship studies on HEPTs by supervised stochastic resonance**

pp 2855–2859

Weimin Guo,\* Xiaofang Hu, Ningping Chu and Chunsheng Yin

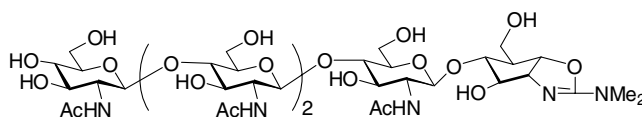


Quantitative structure–activity relationship studies (QSAR) on HEPTs by using a new approach—supervised stochastic resonance (SSR) were reported.

**Chemo-enzymatic synthesis of tetra-*N*-acetyl-chitotetraosyl allosamizoline**

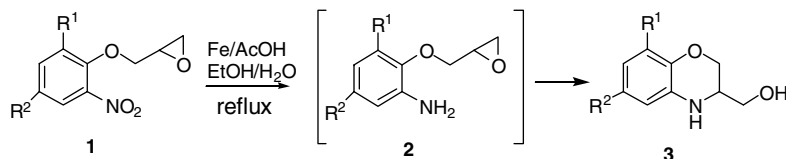
pp 2860–2861

Gang-Liang Huang, Xin-Ya Mei, Hou-Cheng Zhang and Peng-George Wang\*

**Design, synthesis, and preliminary biological evaluation of 2,3-dihydro-3-hydroxymethyl-1,4-benzoxazine derivatives**

pp 2862–2867

Pei-Fu Jiao, Bao-Xiang Zhao,\* Wei-Wei Wang, Qiu-Xia He, Mao-Sheng Wan, Dong-Soo Shin and Jun-Ying Miao\*

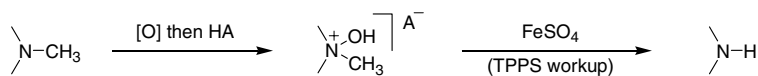


A series of 2,3-dihydro-3-hydroxymethyl-1,4-benzoxazine derivatives (seven compounds) was synthesized and the effects of all of the compounds on HUVEC apoptosis and A549 cell growth were investigated.

### Further investigation of the N-demethylation of tertiary amine alkaloids using the non-classical Polonovski reaction

pp 2868–2871

Shanti Thavaneswaran and Peter J. Scammells\*



The iron salt-mediated Polonovski reaction efficiently N-demethylates certain opiate alkaloids. In this process, the use of the hydrochloride salt of the tertiary *N*-methyl amine oxide was reported to give better yields of the desired N-demethylated product. Herein, we report further investigation into the use of *N*-oxide salts in the iron salt-mediated Polonovski reaction. An efficient approach for the removal of iron salts that greatly facilitates isolation and purification of the *N*-nor product is also described.

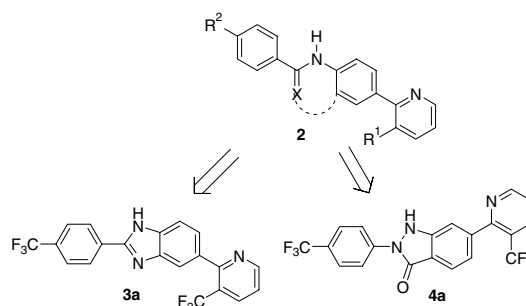


### The search for novel TRPV1-antagonists: From carboxamides to benzimidazoles and indazolones

pp 2872–2876

Stephen Robert Fletcher,\* Edward McIver, Stephen Lewis, Frank Burkamp, Clare Leech, Glenn Mason, Susan Boyce, Denise Morrison, Gillian Richards, Kathy Sutton and Anthony Brian Jones

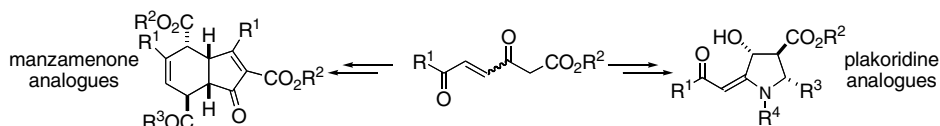
Based on a series of diaryl amides the corresponding inverse amides **2** have been found to be potent TRPV1 receptor antagonists. Benzimidazole (**3**) and indazolone derivatives (**4**) retained good potency in vitro and indazolone **4a** was identified as a novel TRPV1 receptor antagonist suitable for evaluating orally in animal models of analgesia.



### Synthetic analogues of the manzamenones and plakoridines which inhibit DNA polymerase

pp 2877–2881

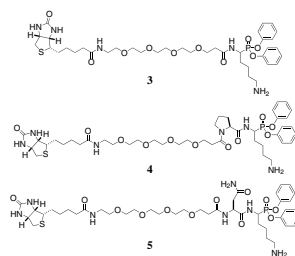
Jeremy R. Doncaster, Laura L. Etchells, Neil M. Kershaw, Ryoichi Nakamura, Hazel Ryan, Ryo Takeuchi, Kengo Sakaguchi, Ali Sardarian and Roger C. Whitehead\*



### Development of activity-based probes for trypsin-family serine proteases

pp 2882–2885

Zhengying Pan,\* Douglas A. Jeffery, Kareem Chegade, Jerlyn Beltman, James M. Clark, Paul Grothaus, Matthew Bogyo\* and Amos Baruch\*

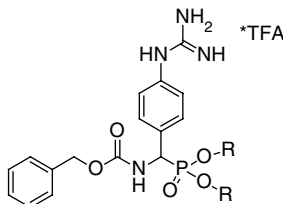


Development and applications of a series of diphenylphosphonate-based probes for the trypsin-like serine proteases are reported.

**Inhibition of trypsin and urokinase by Cbz-amino(4-guanidinophenyl)methanephosphonate aromatic ester derivatives: The influence of the ester group on their biological activity**

pp 2886–2890

Marcin Sieńczyk and Józef Oleksyszyn\*

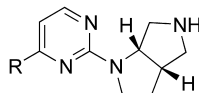


The synthesis and biochemical evaluation of selective and potent diaryl esters of phosphonic-type inhibitors for urokinase and trypsin are reported.

**The identification of pyrimidine-diazabicyclo[3.3.0]octane derivatives as 5-HT<sub>2C</sub> receptor agonists**

pp 2891–2894

Bayard R. Huck,\* Luis Llamas, Michael J. Robarge, Thomas C. Dent, Jianping Song, William F. Hodnick, Chris Crumrine, Alain Stricker-Krongrad, John Harrington, Kurt R. Brunden and Youssef L. Bennani

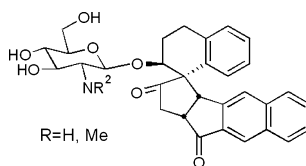


We describe the identification, SAR, and pharmacokinetic profile of a series of nanomolar agonists for 5-HT<sub>2C</sub>, a GPCR that has been implicated as an obesity target.

**Development of new simple molecular probes of DNA bulged structures**

pp 2895–2899

Ziwei Xiao, Lizzy S. Kappen and Irving H. Goldberg\*

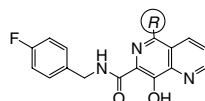


NCSi-gb is a neocarzinostatin chromophore metabolite which binds strongly to certain two-base DNA bulges. New strongly fluorescent analogues of NCSi-gb possessing aminoglycoside appendage on the two-ring system were synthesized and they resemble NSCi-gb in binding affinity and sequence selectivity for two-base DNA bulges.

**A series of 5-aminosubstituted 4-fluorobenzyl-8-hydroxy-[1,6]naphthyridine-7-carboxamide HIV-1 integrase inhibitors**

pp 2900–2904

James P. Guare,\* John S. Wai, Robert P. Gomez, Neville J. Anthony, Samson M. Jolly, Amanda R. Cortes, Joseph P. Vacca, Peter J. Felock, Kara A. Stillmock, William A. Schleif, Gregory Moyer, Lori J. Gabryelski, Lixia Jin, I-Wu Chen, Daria J. Hazuda and Steven D. Young

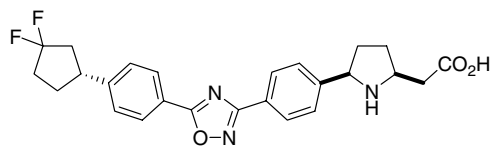


The synthesis and activity of novel 5-aminosubstituted 4-fluorobenzyl-8-hydroxy-[1,6]naphthyridine-7-carboxamide as HIV-1 integrase inhibitors is discussed. A selected derivative was efficacious against replication of simian-human immunodeficiency virus (SHIV) 89.6P in infected rhesus macaques.

**2,5-Disubstituted pyrrolidine carboxylates as potent, orally active sphingosine-1-phosphate (S1P) receptor agonists**

pp 2905–2908

Vincent J. Colandrea,\* Irene E. Legiec, Pei Huo, Lin Yan, Jeffrey J. Hale, Sander G. Mills, James Bergstrom, Deborah Card, Gary Chebret, Richard Hajdu, Carol Ann Keohane, James A. Milligan, Mark J. Rosenbach, Gan-Ju Shei and Suzanne M. Mandala

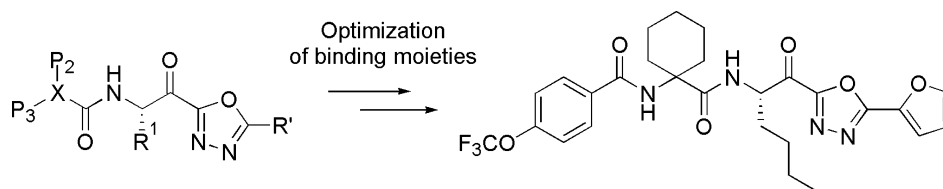
**21**

A series of 2-aryl(pyrrolidine-5-yl)acetic acids (e.g., **21**) were synthesized and evaluated as S1P receptor agonists. Compounds **15–21** were identified with good selectivity over S1P<sub>3</sub> and found to lower peripheral lymphocytes after oral administration in mice.

**Keto-1,3,4-oxadiazoles as cathepsin K inhibitors**

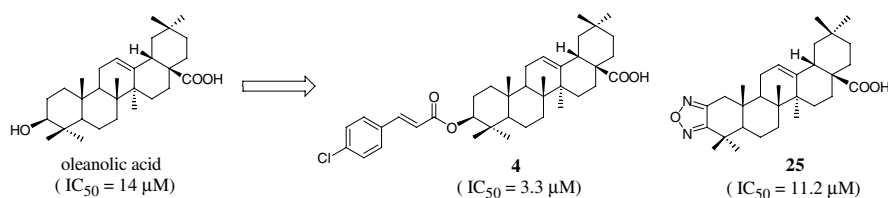
pp 2909–2914

James T. Palmer,\* Bernard L. Hirschbein, Harry Cheung, John McCarter, James W. Janc, Z. Walter Yu and Gregg Wesolowski

**Pentacyclic triterpenes. Part 3: Synthesis and biological evaluation of oleanolic acid derivatives as novel inhibitors of glycogen phosphorylase**

pp 2915–2919

Jun Chen, Jun Liu, Luyong Zhang, Guanzhong Wu, Weiyei Hua, Xiaoming Wu and Hongbin Sun\*

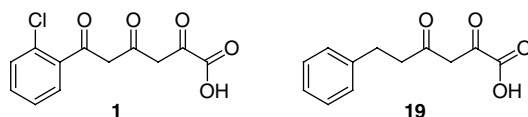


Oleanolic acid and its synthetic derivatives have been identified as novel inhibitors of glycogen phosphorylase. Within this series of compounds, **4** ( $IC_{50} = 3.3 \mu M$ ) is the most potent GP<sub>a</sub> inhibitor.

**Triketoacid inhibitors of HIV-integrase: A new chemotype useful for probing the integrase pharmacophore**

pp 2920–2924

Michael A. Walker,\* Timothy Johnson, Zhuping Ma, Jacques Banville, Roger Remillard, Oak Kim, Yunhui Zhang, Andrew Staab, Henry Wong, Albert Torri, Himadri Samanta, Zeyu Lin, Carol Deminie, Brian Terry, Mark Krystal and Nicholas Meanwell

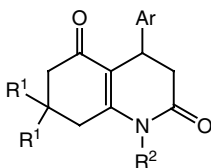


This study reports on the discovery of a new triketoacid-based chemotype that selectively inhibits the strand transfer reaction of HIV-integrase. SAR studies showed that the template binds to integrase in a manner similar to the diketoacid-based inhibitors. Moreover, comparison of the new chemotype to two different diketoacid templates led us to propose two aryl-binding domains in the inhibitor binding site. This information was used to design a new diketoacid template with improved activity against the enzyme.

**New potential biologically active compounds: Design and an efficient synthesis of N-substituted 4-aryl-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-diones under microwave irradiation**

pp 2925–2928

Shujiang Tu,\* Xiaotong Zhu, Jinpeng Zhang, Jianing Xu, Yan Zhang, Qian Wang, Runhong Jia, Bo Jiang, Junyong Zhang and Changsheng Yao

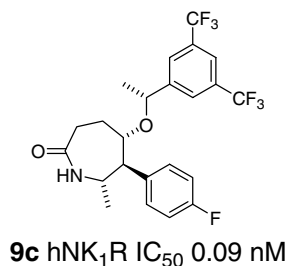


A series of N-substituted 4-aryl-4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione derivatives for biomedical screening were synthesized under microwave irradiation.

**NK<sub>1</sub> antagonists based on seven membered lactam scaffolds**

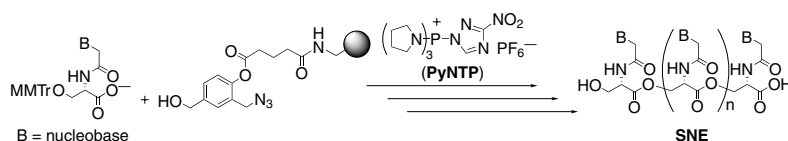
pp 2929–2932

Jason M. Elliott,\* Emma J. Carlson, Gary G. Chicchi, Olivier Dirat, Maria Dominguez, Ute Gerhard, Richard Jelley, A. Brian Jones, Marc M. Kurtz, Kwei lan Tsao and Alan Wheeldon


**Synthesis of a novel ester analog of nucleic acids bearing a serine backbone**

pp 2933–2936

Asako Murata and Takeshi Wada\*

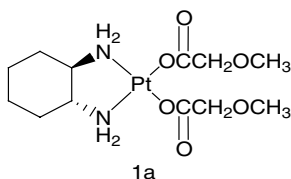


A novel analog of nucleic acids bearing an optically active serine ester backbone: serine-based nucleobase-linked polyester (SNE) was synthesized.

**Novel cisplatin-type platinum complexes and their cytotoxic activity**

pp 2937–2942

Kai Cui, Lianhong Wang, Haibin Zhu, Shaohua Gou\* and Yun Liu



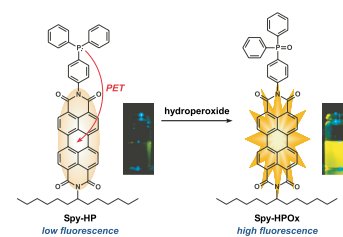
Twelve new cisplatin-type platinum complexes, characteristic of alkoxyacetate as carboxylato ligands, have been synthesized, structurally characterized, and evaluated for their in vitro cytotoxicity against a panel of cultured cell lines. Most of them showed better cytotoxic activity than carboplatin against those selected cell lines.

### Novel fluorescent probe for detecting hydroperoxides with strong emission in the visible range

pp 2943–2946

Nobuaki Soh,\* Tomoyuki Ariyoshi, Tuyoshi Fukaminato, Koji Nakano, Masahiro Irie and Toshihiko Imato\*

A novel fluorescent probe, a swallow-tailed perylene derivative for detecting hydroperoxides (Spy-HP), containing perylene 3,4,9,10-tetracarboxyl bisimide as the main skeleton in the structure, was developed. Spy-HP quantitatively reacted with hydroperoxides to form its oxidized derivative, Spy-HPOx, and emitted an extremely strong fluorescence ( $\Phi \sim 1$ ) in visible range ( $\lambda_{\text{ex}} = 524 \text{ nm}$  and  $\lambda_{\text{em}} = 535 \text{ nm}$ ), as the result of cancelling the photoinduced electron transfer (PET) effect.

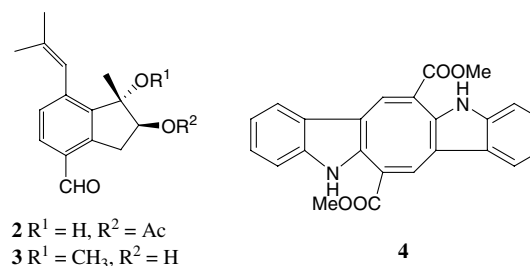


### Two novel aromatic valerenane-type sesquiterpenes from the Chinese green alga *Caulerpa taxifolia*

pp 2947–2950

Shui-Chun Mao, Yue-Wei Guo\* and Xu Shen

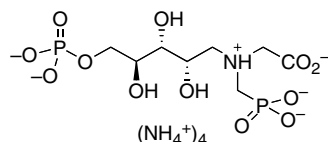
Caulerpals A (**2**) and B (**3**), two novel sesquiterpenes possessing an uncommon aromatic valerenane-type carbon skeleton, along with one known metabolite, caulerpin (**4**), have been isolated from the Chinese green alga *Caulerpa taxifolia* (Vahl) C. Agardh. Their structures and relative stereochemistry were elucidated on the basis of extensive spectroscopic analysis. Compounds **2–4** were evaluated for their inhibitory activity against hPTP1B and the result showed that only compound **4** had a strong PTP1B inhibitory activity with an  $\text{IC}_{50}$  value of  $3.77 \mu\text{M}$ .



### Synthesis and evaluation of a mechanism-based inhibitor of a 3-deoxy-D-arabino heptulosonate 7-phosphate synthase

pp 2951–2954

Scott R. Walker and Emily J. Parker\*

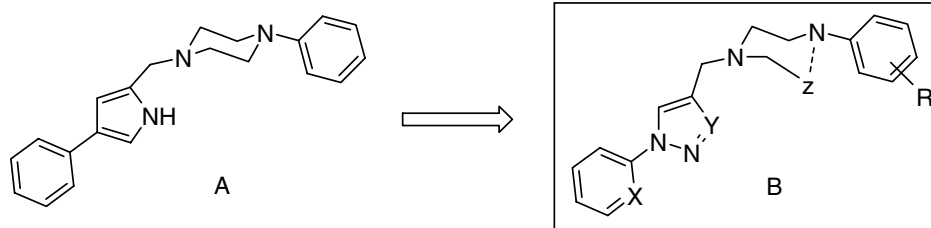


The first mechanism-based inhibitor of a 3-deoxy-D-arabino heptulosonate 7-phosphate (DAH7P) synthase has been synthesised in 12 steps from D-arabinose, and has been found to be a very slow binding inhibitor of *Escherichia coli* DAH7P synthase.

### Synthesis and biological investigations of dopaminergic partial agonists preferentially recognizing the D4 receptor subtype

pp 2955–2959

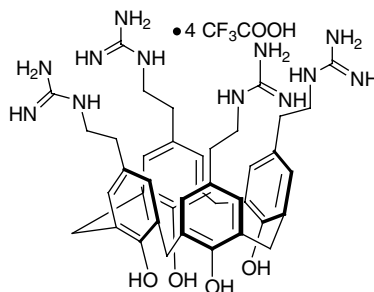
Stefan Löber, Harald Hübner and Peter Gmeiner\*



**Functional organisation and gain of activity: The case of the antibacterial tetra-*para*-guanidinoethyl-calix[4]arene**

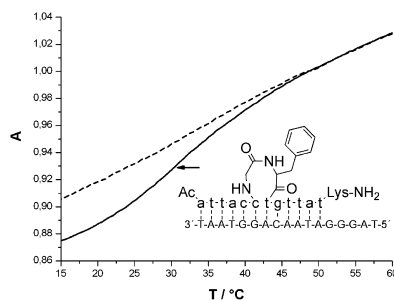
pp 2960–2963

Maxime Mourer, Raphaël E. Duval, Chantal Finance and Jean-Bernard Regnouf-de-Vains\*


**Insertion of an internal dipeptide into PNA oligomers: Thermal melting studies and further functionalization**

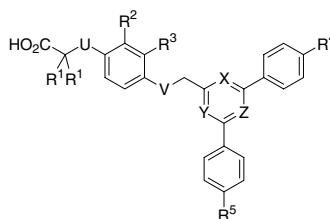
pp 2964–2968

Tim Kersebohm, Srećko I. Kirin and Nils Metzler-Nolte\*


**1,3,5-Trisubstituted aryls as highly selective PPAR $\delta$  agonists**

pp 2969–2973

Robert Epple,\* Mihai Azimioara, Ross Russo, Badry Bursulaya, Shin-Shay Tian, Andrea Gerken and Maya Iskandar

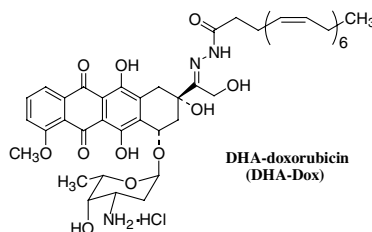


A series of highly potent and selective PPAR agonists is reported.


**Synthesis and preliminary antitumor activity evaluation of a DHA and doxorubicin conjugate**

pp 2974–2977

Yuqiang Wang,\* Lianfa Li, Wei Jiang, Zhaoqi Yang and Zaijun Zhang



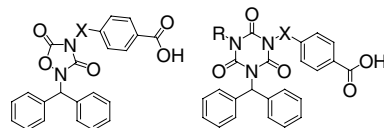
Synthesis of a DHA and doxorubicin conjugate is reported.



**1,2,4-Oxadiazolidin-3,5-diones and 1,3,5-triazin-2,4,6-triones as cytosolic phospholipase A<sub>2</sub> inhibitors**

pp 2978–2981

Ariamala Gopalsamy,\* Hui Yang, John W. Ellingboe, John C. McKew, Steve Tam, Diane Joseph-McCarthy, Wen Zhang, Marina Shen and James D. Clark



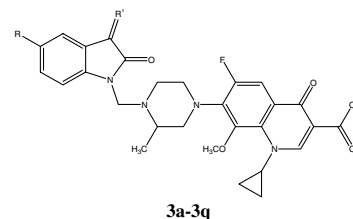
Novel scaffolds based on 1,2,4-oxadiazolidin-3,5-dione and 1,3,5-triazin-2,4,6-trione are described as cytosolic phospholipase A<sub>2</sub> substrate mimetics.

**Gatifloxacin derivatives: Synthesis, antimycobacterial activities, and inhibition of *Mycobacterium tuberculosis* DNA gyrase**

pp 2982–2985

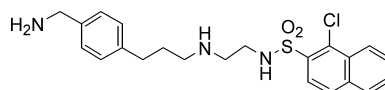
Dharmarajan Sriram,\* Alexandra Aubry, Perumal Yogeeswari and L. M. Fisher

Among the synthesized compounds, 1-cyclopropyl-6-fluoro-8-methoxy-7-[[[N<sup>4</sup>-[1'-(5-isatinyl-β-semicarbazoyl)methyl]3-methyl]N<sup>1</sup>-piperazinyl]-4-oxo-1,4-dihydro-3-quinoline carboxylic acid (**3d**) was found to be the most active compound in vitro with an MIC of 0.0125 μg/mL against MTB and MTR-TB. In the in vivo animal model **3d** decreased the bacterial load in lung and spleen tissues with 3.62- and 3.76-log<sub>10</sub> protections, respectively. Compound **3d** was also found to be equally active as gatifloxacin in the inhibition of the supercoiling activity of wild-type *Mycobacterium tuberculosis* DNA gyrase with an IC<sub>50</sub> of 3.0 μg/mL.


**Synthesis and evaluation of 4-substituted benzylamine derivatives as β-tryptase inhibitors**

pp 2986–2990

Yutaka Miyazaki,\* Yutaka Kato, Tadashi Manabe, Hiroyasu Shimada, Masashi Mizuno, Takayuki Egusa, Munetaka Ohkouchi, Ikuya Shiromizu, Tomokazu Matsusue and Ichiro Yamamoto

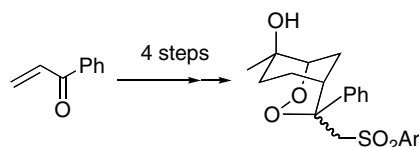

**15h** IC<sub>50</sub> = 5 nM

Synthesis and structure–activity relationships of β-tryptase inhibitors are described.

**Diels–Alder/thiol–olefin co-oxygenation approach to antimalarials incorporating the 2,3-dioxabicyclo[3.3.1]nonane pharmacophore**

pp 2991–2995

Paul M. O'Neill,\* Edite Verissimo, Stephen A. Ward, Jill Davies, Edward E. Korshin, Nuna Araujo, Matthew D. Pugh, M. Lurdes S. Cristiano, Paul A. Stocks and Mario D. Bachi\*

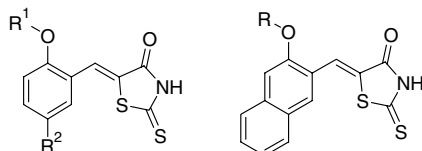


A Diels–Alder/thiol–olefin co-oxygenation approach to the synthesis of novel bicyclic endoperoxides **17a–22b** is reported. Some of these bicyclic endoperoxides (e.g., **17b**, **19b**, **22a** and **22b**) have potent nanomolar antimalarial activity equivalent to that of the synthetic antimalarial agent artefene.

**Synthesis and biological evaluation of rhodanine derivatives as PRL-3 inhibitors**

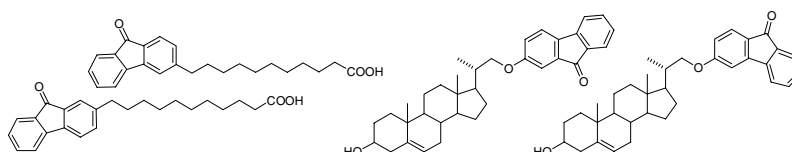
pp 2996–2999

Jin Hee Ahn, Seung Jun Kim, Woul Seong Park, Sung Yun Cho, Jae Du Ha, Sung Soo Kim, Seung Kyu Kang, Dae Gwin Jeong, Suk-Kyeong Jung, Sang-Hyeup Lee, Hwan Mook Kim, Song Kyu Park, Ki Ho Lee, Chang Woo Lee, Seong Eon Ryu\* and Joong-Kwon Choi\*

**Preparation and biochemical evaluation of fluorenone-containing lipid analogs**

pp 3000–3004

Thomas A. Spencer,\* Pingzhen Wang, Janeta V. Popovici-Müller, Ithan D. Peltan, Phoebe E. Fielding and Christopher J. Fielding



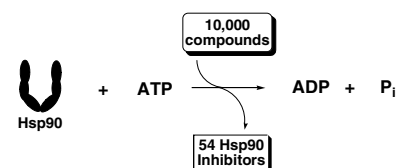
Syntheses are described of analogs of fatty acids and cholesterol containing the fluorenone moiety, which is both photoactivable and fluorescent. Evidence is presented that the sterol analogs can substitute successfully for cholesterol in living cells.

**High-throughput screening for Hsp90 ATPase inhibitors**

pp 3005–3008

Christopher Avila, M. Kyle Hadden, Zeqiang Ma, Boris A. Kornilayev, Qi-Zhuang Ye and Brian S. J. Blagg\*

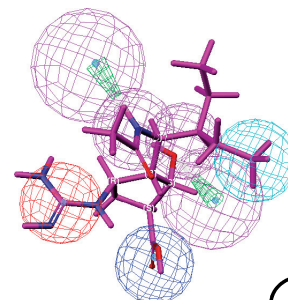
Recently, we reported a useful assay for the determination of Hsp90 ATPase activity. Using this assay, high-throughput screening of ~10,000 compounds was performed to determine the feasibility of this assay on large scale. Results from high-throughput screening indicated that the assay was reproducible (av Z-factor = 0.80) and identified 0.57% of the compounds as Hsp90 inhibitors that exhibited IC<sub>50</sub>s less than 20 μM. The structures of several of these inhibitory scaffolds are reported along with their IC<sub>50</sub> values.

**Neuraminidase pharmacophore model derived from diverse classes of inhibitors**

pp 3009–3014

Jian Zhang, KunQian Yu, Weiliang Zhu\* and Hualiang Jiang\*

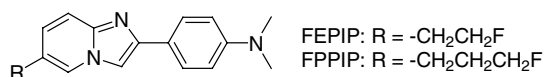
A quantitative pharmacophore hypothesis for AIV neuraminidase inhibitors was built based on 22 compounds with great molecular diversity and bioactivity, and validated using 88 compounds to be highly predictive.



**Synthesis and evaluation of two  $^{18}\text{F}$ -labeled imidazo[1,2-*a*]pyridine analogues as potential agents for imaging  $\beta$ -amyloid in Alzheimer's disease**

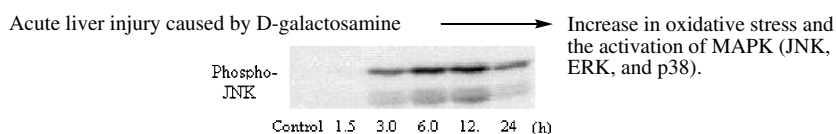
pp 3015–3018

Fanxing Zeng, Jeanine A. Southerland, Ronald J. Voll, John R. Votaw, Larry Williams, Brian J. Ciliax, Allan I. Levey and Mark M. Goodman\*


**Activation of mitogen activated protein kinase (MAPK) during D-galactosamine intoxication in the rat liver**

pp 3019–3022

Hitomi Nishioka, Terumi Kishioka, Chinatsu Iida, Kozue Fujii, Ikuyo Ichi and Shosuke Kojo\*

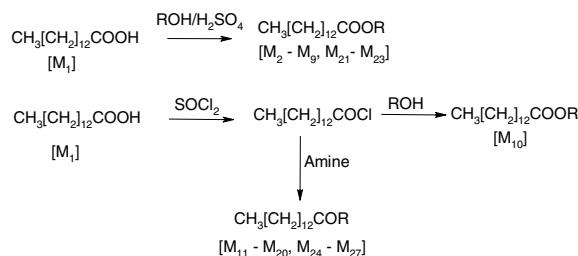


Oxidative stress and the activation of JNK and ERK took place almost simultaneously in the rat liver by intraperitoneal administration of D-galactosamine, followed by the activation of p38 MAPK.

**Design, synthesis, antibacterial, and QSAR studies of myristic acid derivatives**

pp 3023–3029

Balasubramanian Narasimhan, Vishnukant Mourya and Avinash Dhake\*

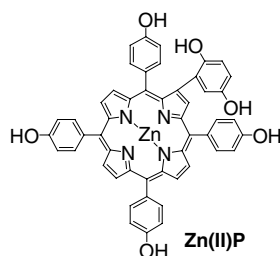


QSAR study of synthesized myristic acid derivatives as antibacterial agents indicated the importance of topological parameters  ${}^2\chi^v$  and  ${}^0\chi^v$  in contribution to antibacterial activity.

**Zinc(II) and copper(II) complexes of  $\beta$ -substituted hydroxylporphyrins as tumor photosensitizers**

pp 3030–3033

Qimao Huang, Zhiquan Pan,\* Ping Wang, Zhangping Chen, Xiaolian Zhang and Hansheng Xu



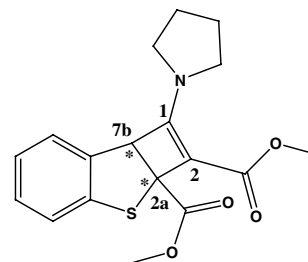
Novel photosensitizers hydroxylporphyrins were synthesized and characterized. The preliminary biological activity studies show that Zn(II)P having high anti-tumor activity(in vitro).

### New HIV-1 reverse transcriptase inhibitors based on a tricyclic benzothiophene scaffold: Synthesis, resolution, and inhibitory activity

pp 3034–3038

Krzysztof Krajewski, Yijun Zhang, Damon Parrish, Jeffrey Deschamps, Peter P. Roller\* and Vinay K. Pathak\*

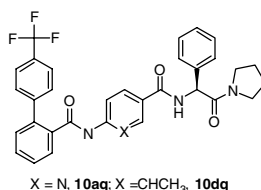
The synthesis and HIV-1 reverse transcriptase inhibitory activity of dimethyl-1-(1-piperidinyl)cyclobuta[*b*][1]-benzothiophene-2,2a(7*bH*)-dicarboxylate (NSC-380292) enantiomers and its structural analogs are reported.



### Discovery of potent and orally active MTP inhibitors as potential anti-obesity agents

pp 3039–3042

Jin Li,\* Peter Bertinato, Hengmiao Cheng, Bridget M. Cole, Brian S. Bronk, Burton H. Jaynes, Anne Hickman, Michelle L. Haven, Nicole L. Kolosko, Chris J. Barry and Tara B. Manion

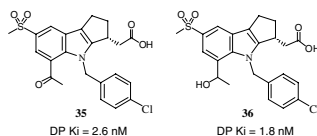


Structure activity relationship (SAR) studies of a novel class of MTP inhibitors are described. A number of novel MTP inhibitors have been identified with single digit nanomolar potency. Analogues **10aq** and **10dq** demonstrated in vivo efficacy in a murine gut retention assay.

### Identification of an indole series of prostaglandin D<sub>2</sub> receptor antagonists

pp 3043–3048

Claudio F. Sturino,\* Nicolas Lachance, Michael Boyd, Carl Berthelette, Marc Labelle, Lianhai Li, Bruno Roy, John Scheiget, Nancy Tsou, Christine Brideau, Elizabeth Cauchon, Marie-Claude Carriere, Danielle Denis, Gillian Greig, Stacia Kargman, Sonia Lamontagne, Marie-Claude Mathieu, Nicole Sawyer, Deborah Slipetz, Gary O'Neill, Zhaoyin Wang, Robert Zamboni, Kathleen M. Metters and Robert N. Young

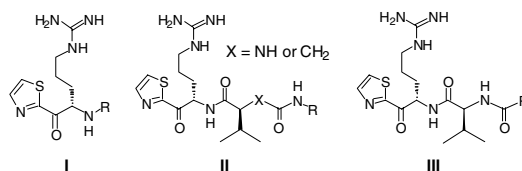


A novel indole series of PGD<sub>2</sub> receptor (DP receptor) antagonists are presented. Optimization led to the identification of the potent and selective DP receptor antagonists **35** and **36**.

### Synthesis, SAR exploration, and X-ray crystal structures of factor XIa inhibitors containing an α-ketothiazole arginine

pp 3049–3054

Hongfeng Deng,\* Thomas D. Bannister, Lei Jin, Robert E. Babine, Jesse Quinn, Pamela Nagafuji, Cassandra A. Celatka, Jian Lin, Tsvetelina I. Lazarova, Michael J. Rynkiewicz, Frank Bibbins, Pramod Pandey, Joan Gorga, Harold V. Meyers, Sherin S. Abdel-Meguid and James E. Strickler

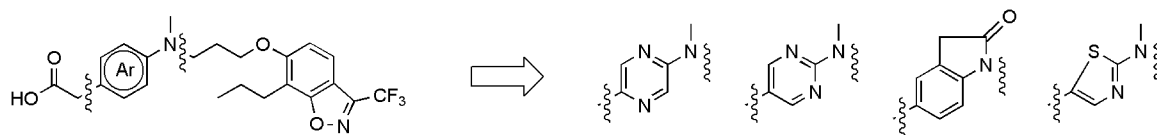


A series of small peptidomimetic molecules was designed and synthesized, and their co-crystal structures with factor XIa were studied in an effort to develop smaller, less peptidic inhibitors as antithrombotic agents.

**SAR studies: Designing potent and selective LXR agonists**

pp 3055–3060

Jason W. Szewczyk,\* Shaei Huang, Jayne Chin, Jenny Tian, Lyndon Mitnaul, Raymond L. Rosa, Larry Peterson, Carl P. Sparrow and Alan D. Adams

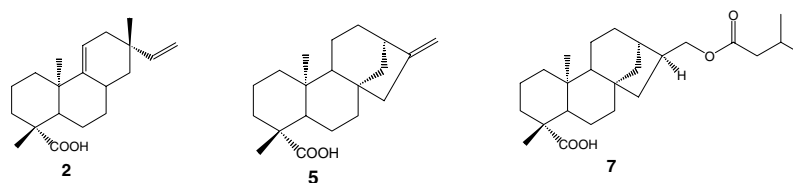


Lead screening at Merck identified a potent, dual LXR/PPAR agonist. SAR optimization developed a series of LXR specific heterocyclic agonists having excellent LXR affinity, good in vivo, potency and high selectivity versus other nuclear hormone receptors.

**Inhibition of protein tyrosine phosphatase 1B by diterpenoids isolated from *Acanthopanax koreanum***

pp 3061–3064

MinKyun Na, Won Keun Oh, Young Ho Kim, Xing Fu Cai, SoHee Kim, Bo Yeon Kim and Jong Seog Ahn\*

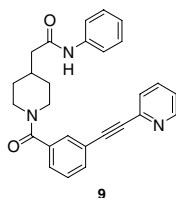


Bioassay-guided fractionation of the CH<sub>2</sub>Cl<sub>2</sub>-soluble fraction led to the isolation of three PTP1B inhibitory diterpenoids, acanthoic acid (2), *ent*-kaur-16-en-19-oic acid (5), and 16 $\alpha$ H,17-isovaleryloxy-*ent*-kauran-19-oic acid (7), along with their five derivatives.

**Diarylacetylene piperidinyl amides as novel anxiolytics**

pp 3065–3067

Cheryl P. Kordik,\* Chi Luo, Maryann Gutherman, Anil H. Vaidya, Daniel I. Rosenthal, Jeffrey J. Crooke, Sandra L. McKenney, Carlos R. Plata-Salaman and Allen B. Reitz

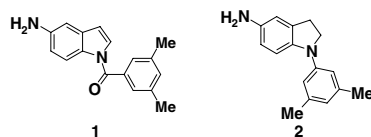


The chemistry and activity of anxiolytic diarylacetylene piperidine **9** is described.

**Anti-angiogenic activity of basic-type, selective cyclooxygenase (COX)-1 inhibitors**

pp 3068–3072

Hiroko Sano, Tomomi Noguchi, Atsushi Miyajima, Yuichi Hashimoto and Hiroyuki Miyachi\*

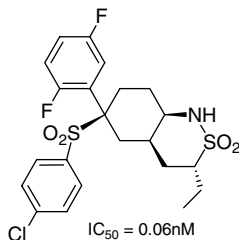


Indole- and indoline-type basic COX-1-selective competitive inhibitors were found to possess anti-angiogenic activity.

**3,4-Fused cyclohexyl sulfones as  $\gamma$ -secretase inhibitors**

pp 3073–3077

Duncan Shaw,\* Jonathan Best, Kevin Dinnell, Alan Nadin, Mark Shearman, Christine Pattison, James Peachey, Michael Reilly, Brian Williams, Jonathan Wrigley and Timothy Harrison

The identification of a potent  $\gamma$ -secretase inhibitor, for example (ED<sub>50</sub> = 0.06 nM), is reported.**OTHER CONTENTS**

Corrigenda

p 3078, 3079

Summary of instructions to authors

p I

\*Corresponding author

①\* Supplementary data available via ScienceDirect

**COVER**

View of the crystal structure of the DB819-d(CGCGAATTCGCG)<sub>2</sub> complex, looking down the minor groove of the DNA (see Campbell, N.H.; Evans, D.A.; Lee, M.P.H.; Parkinson, G.N.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 15.). The DB819 molecule is shown in space-filling mode. Visualisation produced with the VMD program. [Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* **1996**, *14*, 33.]

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ISSN 0960-894X