

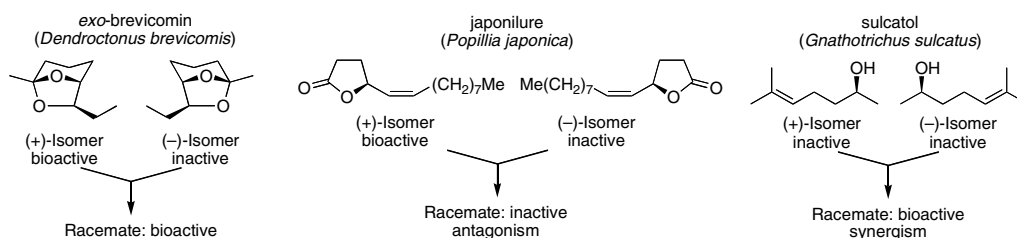
## Contents

### REVIEW

#### Significance of chirality in pheromone science

Kenji Mori\*

pp 7505–7523

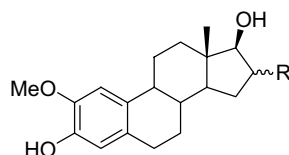


### ARTICLES

#### Synthesis and structure–activity relationships of 16-modified analogs of 2-methoxyestradiol

pp 7524–7537

Gregory E. Agoston,\* Jamshed H. Shah, Theresa M. LaVallee, Xiaoguo Zhan, Victor S. Pribluda and Anthony M. Treston

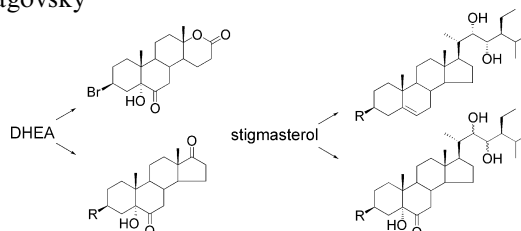


A series of 16-substituted 2-methoxyestradiol analogs were synthesized and evaluated for antiproliferative activity, estrogenicity, and the ability to form glucuronide and sulfonate conjugates.

#### Syntheses of immunomodulating androstanes and stigmastanes: Comparison of their TNF- $\alpha$ inhibitory activity

pp 7538–7544

Javier A. Ramírez,\* Andrea C. Bruttomesso, Flavia M. Michelini, Sofía L. Acebedo, Laura E. Alché and Lydia R. Galagovsky



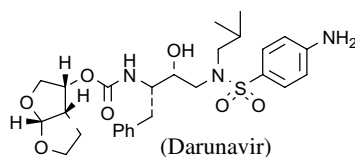
Several synthetic stigmastanes and androstane were able to inhibit the TNF- $\beta$  production. Some of them were shown to be more potent inhibitors than DHEA.



**Darunavir, a conceptually new HIV-1 protease inhibitor for the treatment of drug-resistant HIV**

pp 7576–7580

Arun K. Ghosh,\* Zachary L. Dawson and Hiroaki Mitsuya

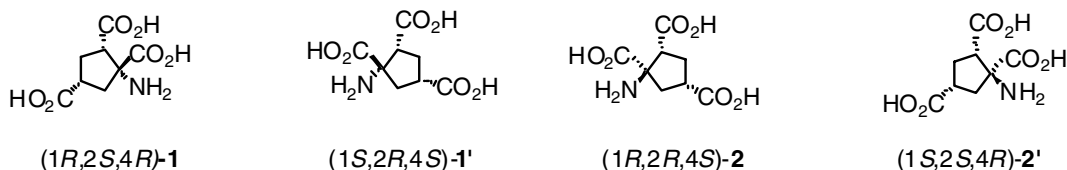


This perspective article describes our structure-based design efforts targeting the protein-backbone of HIV-1 protease to combat drug-resistance. Darunavir has been recently approved for the treatment of drug-resistant HIV.

**1-Aminocyclopentane-1,2,4-tricarboxylic acids screening on glutamatergic and serotonergic systems**

pp 7581–7589

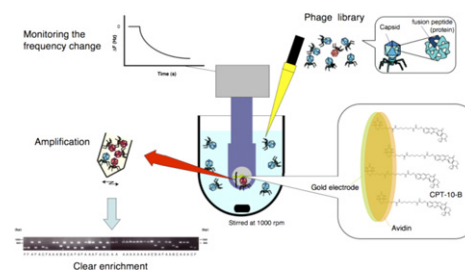
Maria Luisa Gelmi,\* Francesco Caputo, Francesca Clerici, Sara Pellegrino, Gino Giannaccini, Laura Betti, Laura Fabbrini, Lara Schmid, Lionella Palego and Antonio Lucacchini

**Identification of C10 biotinylated camptothecin (CPT-10-B) binding peptides using T7 phage display screen on a QCM device**

pp 7590–7598

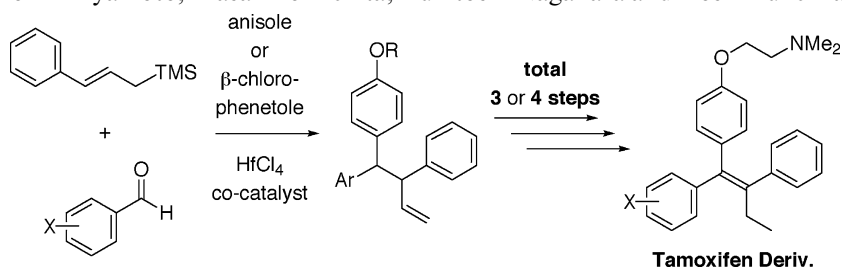
Yoichi Takakusagi, Kaori Takakusagi, Kouji Kuramochi, Susumu Kobayashi, Fumio Sugawara and Kengo Sakaguchi\*

A screening of peptide that binds to CPT-10-B was carried out using T7 phage display method on a QCM device.

**An expeditious synthesis of tamoxifen, a representative SERM (selective estrogen receptor modulator), via the three-component coupling reaction among aromatic aldehyde, cinnamyltrimethylsilane, and  $\beta$ -chlorophenetole**

pp 7599–7617

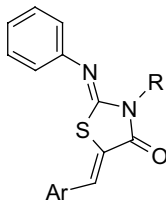
Isamu Shiina,\* Yoshiyuki Sano, Kenya Nakata, Masahiko Suzuki, Toshikazu Yokoyama, Akane Sasaki, Tomoko Orikasa, Tomomi Miyamoto, Masahiko Ikekita, Yukitoshi Nagahara and Yoshimune Hasome



**Synthesis and in vitro evaluation of 5-arylidene-3-hydroxyalkyl-2-phenylimino-4-thiazolidinones with antidegenerative activity on human chondrocyte cultures**

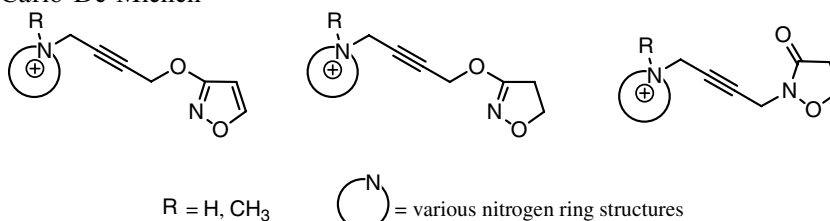
pp 7618–7625

Rosaria Ottanà,\* Rosanna Maccari, Rosella Ciurleo, Maria Gabriella Vigorita, Anna Maria Panico, Venera Cardile, Floriana Garufi and Simone Ronsisvalle


**Novel oxotremorine-related heterocyclic derivatives: Synthesis and in vitro pharmacology at the muscarinic receptor subtypes**

pp 7626–7637

Clelia Dallanocce,\* Marco De Amici, Elisabetta Barocelli, Simona Bertoni, Bryan L. Roth, Paul Ernsberger and Carlo De Micheli

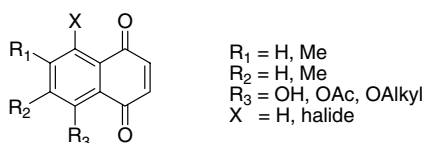


A series of nonquaternized and quaternized butynyl derivatives related to Oxotremorine was synthesized, and tested at muscarinic receptor subtypes (mAChRs).

**Activity of 7-methyljuglone derivatives against *Mycobacterium tuberculosis* and as subversive substrates for mycothiol disulfide reductase**

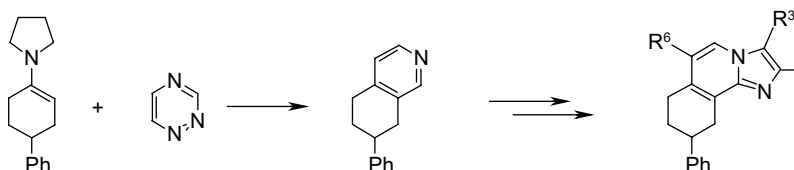
pp 7638–7646

Anita Mahapatra, Sannah P. N. Mativandlela, B. Binneman, P. B. Fourie, Chris J. Hamilton,\* J. J. M. Meyer, F. van der Kooy, Peter Houghton and Namrita Lall\*


**Preparation of tetrahydroimidazo[2,1-*a*]isoquinolines and their use as inhibitors of gastric acid secretion**

pp 7647–7660

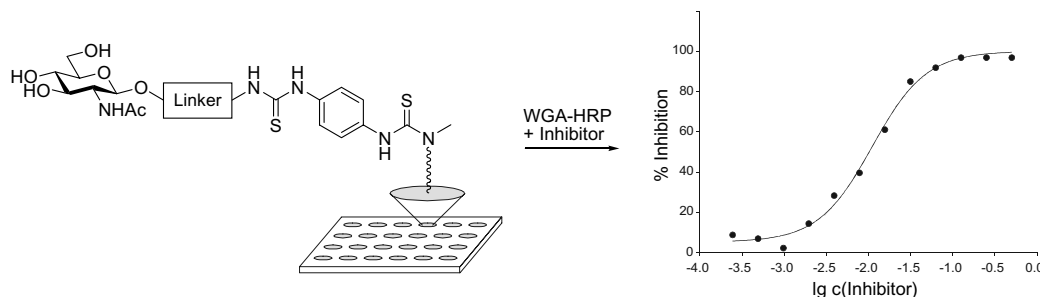
Andreas Marc Palmer,\* Burkhard Grobbel, Christof Brehm, Peter Jan Zimmermann, Wilh Buhr, Martin Philipp Feth, Hans Christof Holst and Wolfgang Alexander Simon


 A series of novel tetrahydroimidazo[2,1-*a*]isoquinolines were prepared based on a hetero Diels–Alder reaction between an enamine and 1,2,4-triazine as key step and their inhibiting effect on the gastric proton pump enzyme was assessed.


## Probing multivalent carbohydrate–lectin interactions by an enzyme-linked lectin assay employing covalently immobilized carbohydrates

pp 7661–7676

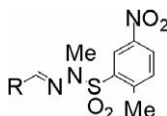
Caroline Maierhofer, Katja Rohmer and Valentin Wittmann\*



## Synthesis, biological evaluation and molecular modelling of sulfonylhydrazides as selective PI3K p110 $\alpha$ inhibitors

pp 7677–7687

Jackie D. Kendall,\* Gordon W. Rewcastle, Raphael Frederick, Claire Mawson, William A. Denny, Elaine S. Marshall, Bruce C. Baguley, Claire Chaussade, Shaun P. Jackson and Peter R. Shepherd

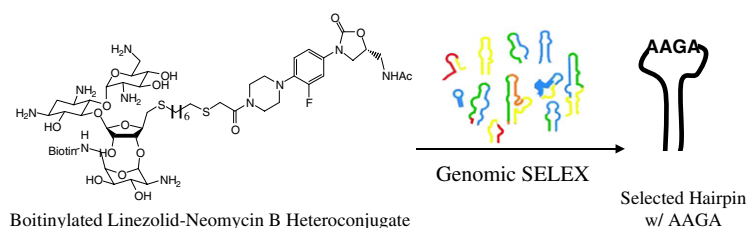


A novel series of sulfonylhydrazides were synthesised and evaluated for inhibition of isoforms of PI3K, and inhibition of cell proliferation. Molecular modelling helps to rationalise the observed SAR.

## Elucidation of the RNA target of linezolid by using a linezolid–neomycin B heteroconjugate and genomic SELEX

pp 7688–7695

Hyun Jin Kim, Miyun Kwon and Jaehoon Yu\*

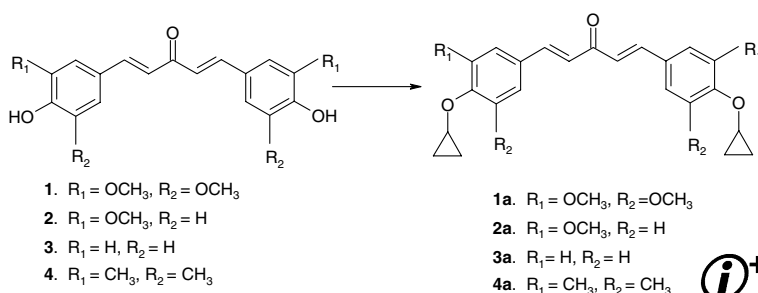


## In vivo growth inhibitory and anti-angiogenic effects of synthetic novel dienone cyclopropoxy curcumin analogs on mouse Ehrlich ascites tumor

pp 7696–7703

H. Chandru, A. C. Sharada,\* B. K. Bettadaiah, C. S. Ananda Kumar, K. S. Rangappa, Sunila and K. Jayashree

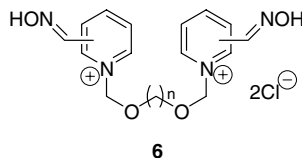
In the present study, four novel dienone cyclopropoxy curcumin analogs **1a–4a** were synthesized by nucleophilic substitution reaction with cyclopropyl bromide. The tumor inhibitory and anti-angiogenic effects of the synthetic compounds were studied on mouse Ehrlich ascites tumor (EAT) in vivo. The compounds **1a–4a** increased the life span (% ILS) of EAT bearing mice with corresponding significant reduction in ascites volume and cell number and induced apoptotic bodies in EAT cells. Anti-angiogenic studies of the compounds demonstrated significant reduction of microvessel density (MVD) in the peritoneum wall sections of mice and induced avascular zone in CAM model.



### New oxime reactivators connected with $\text{CH}_2\text{O}(\text{CH}_2)_n\text{OCH}_2$ linker and their reactivation potency for organophosphorus agents-inhibited acetylcholinesterase

pp 7704–7710

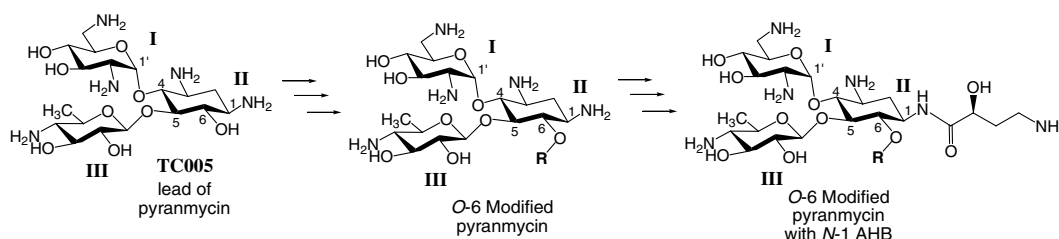
Garp Yeol Yang, Kyung-Ae Oh, No-Joong Park and Young-Sik Jung\*



### Synthesis and antibacterial activity of pyranmycin derivatives with *N*-1 and *O*-6 modifications

pp 7711–7719

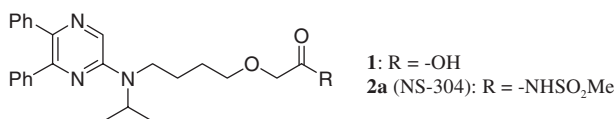
Jie Li, Fang-I Chiang, Hsiao-Nung Chen and Cheng-Wei Tom Chang\*



### Synthesis and evaluation of *N*-acylsulfonamide and *N*-acylsulfonylurea prodrugs of a prostacyclin receptor agonist

pp 7720–7725

Akio Nakamura, Tetsuhiro Yamada and Tetsuo Asaki\*

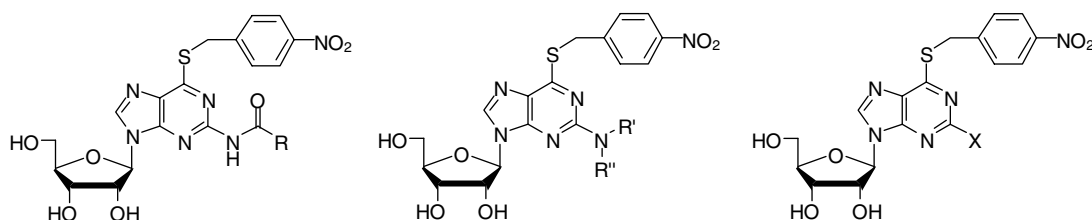


*N*-Acylsulfonamide and *N*-acylsulfonylurea derivatives of prostacyclin receptor agonist **1** were evaluated as prodrugs of **1** in vitro and in vivo. These types of analogues, including NS-304 (**2a**), were found to have potential as new prostacyclin receptor agonist prodrugs with long-lasting activity.

### Novel *C*<sup>2</sup>-purine position analogs of nitrobenzylmercaptapurine riboside as human equilibrative nucleoside transporter 1 inhibitors

pp 7726–7737

Amol Gupte and John K. Buolamwini\*



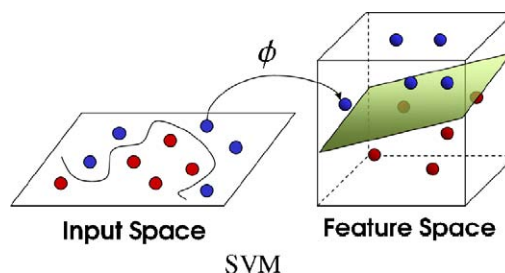
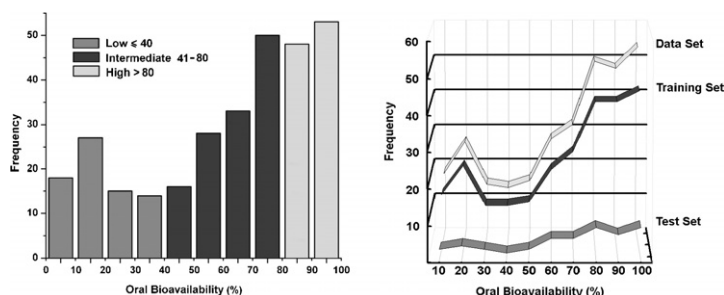
The synthesis and flow cytometric investigation of structure–activity relationship of new *C*<sup>2</sup>-purine position substituted analogs of NBMPR as inhibitors of the human equilibrative nucleoside transporter (hENT1) is reported.

## pp 7738–7745

# A novel QSAR model for prediction of apoptosis-inducing activity of 4-aryl-4-H-chromenes based on support vector machine

pp 7746–7754

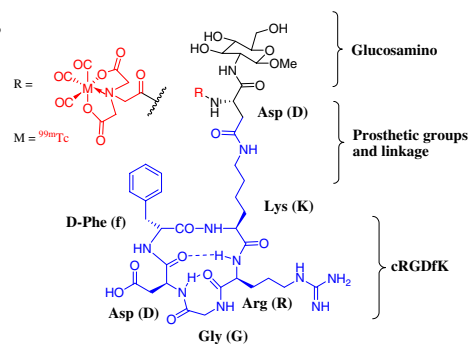
Support vector machine (SVM) as a new nonlinear feature mapping method was applied together with genetic algorithm as a variable subset selection techniques for modeling of the induction of apoptosis by 4-aryl-4-H-chromenes with the descriptors calculated from the molecular structure alone using a quantitative structure–activity relationship technique.



## Synthesis of Tc-99m labeled glucosamino-Asp-cyclic(Arg-Gly-Asp-D-Phe-Lys) as a potential angiogenesis imaging agent

pp 7755–7764

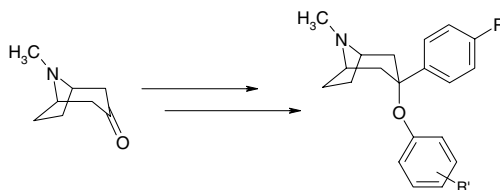
Byung Chul Lee, Hyun Ju Sung, Ji Sun Kim, Kyung-Ho Jung,  
Yeareon Seong Choe, Kyung-Han Lee and Dae Yoon Chi\*



### Synthesis of some tropane derivatives of anticipated activity on the reuptake of norepinephrine and/or serotonin

pp 7765–7772

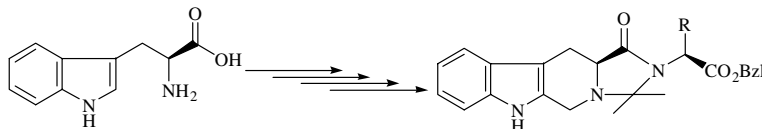
Mona M. Hanna,\* Nahed M. Eid, Riham F. George and Hani M. Safwat



**Dual-acting agents that possess reversing resistance and anticancer activities: Design, synthesis, MES-SA/Dx5 cell assay, and SAR of Benzyl 1,2,3,5,11,11a-hexahydro-3,3-dimethyl-1-oxo-6H-imidazo[3',4':1,2]pyridin[3,4-b]indol-2-substitutedacetates**

pp 7773–7788

Jiawang Liu, Guohui Cui, Ming Zhao,\* Chunying Cui, Jingfang Ju\* and Shiqi Peng\*

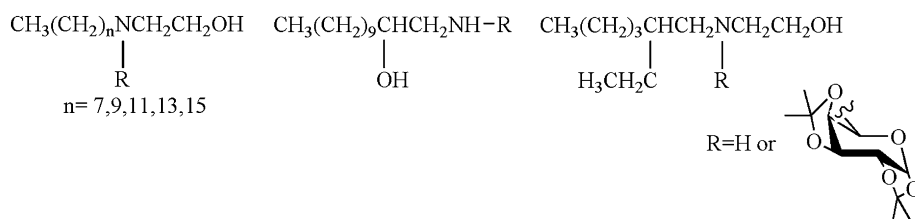


Wherein R represents the side chain of L-amino acids.

**Preparation and antitubercular activities of alkylated amino alcohols and their glycosylated derivatives**

pp 7789–7794

Aline F. Taveira, Mireille Le Hyaric, Elaine F. C. Reis, Débora P. Araújo, Ana Paula Ferreira, Maria Aparecida de Souza, Livia L. Alves, Maria C. S. Lourenço, Felipe Rodrigues C. Vicente and Mauro V. de Almeida\*



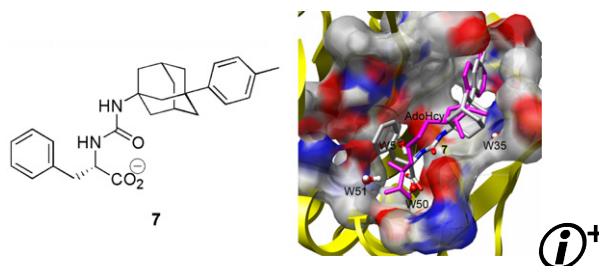
N- and C-alkylated amino alcohols and their glycosylated analogues were prepared and evaluated for their antitubercular activity.

**Virtual screening and bioassay study of novel inhibitors for dengue virus mRNA cap (nucleoside-2'O)-methyltransferase**

pp 7795–7802

Victor B. Luzhkov, Barbara Selisko, Anneli Nordqvist, Frédéric Peyrane, Etienne Decroly, Karine Alvarez, Anders Karlen, Bruno Canard and Johan Åqvist\*

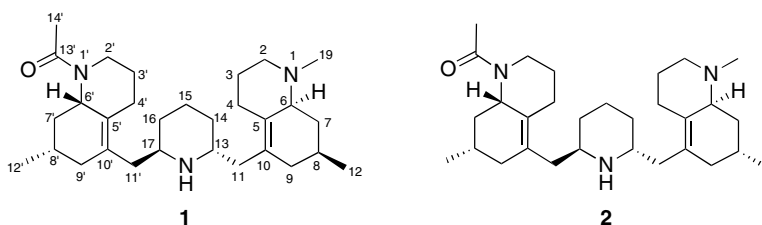
Using a combination of virtual screening and bioassay activity testing, a novel inhibitor of a flavivirus mRNA capping methyltransferase has been identified.



**Cryptadines A and B, novel C<sub>27</sub>N<sub>3</sub>-type pentacyclic alkaloids from *Lycopodium cryptomerinum***

pp 7803–7808

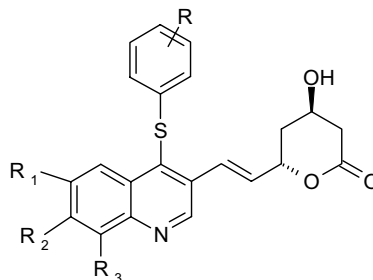
Koichiro Koyama, Yusuke Hirasawa, Jun'ichi Kobayashi\* and Hiroshi Morita\*



### Synthesis and HMG CoA reductase inhibition of 4-thiophenyl quinolines as potential hypocholesterolemic agents

pp 7809–7829

Zhengyan Cai,\* Weicheng Zhou and Lixin Sun



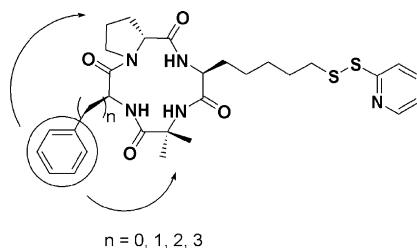
Novel 4-thiophenyl quinoline-based HMG CoA reductase inhibitors were synthesized. Some compounds showed great potency in vitro.



### Molecular design of histone deacetylase inhibitors by aromatic ring shifting in chlamydocin framework

pp 7830–7839

Gururaj M. Shivashimpi, Satoshi Amagai, Tamaki Kato, Norikazu Nishino,\* Satoko Maeda, Tomonori G. Nishino and Minoru Yoshida

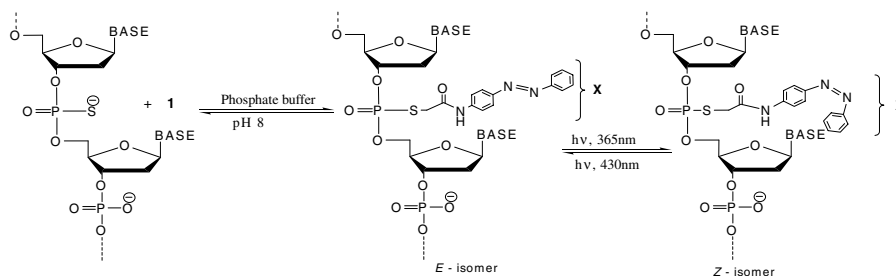


### Photomodulation of PS-modified oligonucleotides containing azobenzene substituent at pre-selected positions in phosphate backbone

pp 7840–7849

Satyakam Patnaik, P. Kumar, B. S. Garg, R. P. Gandhi and K. C. Gupta\*

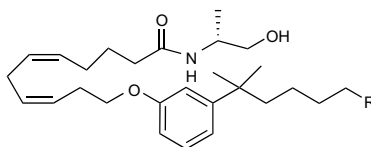
A new protocol has been developed for incorporation of photoisomerizable azobenzene substituent into synthetic PS-oligonucleotides.



### Novel, potent THC/anandamide (hybrid) analogs

pp 7850–7864

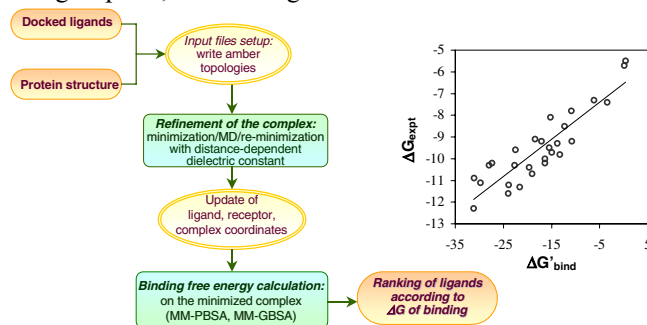
Caryl Bourne, Sucharita Roy, Jenny L. Wiley, Billy R. Martin, Brian F. Thomas, Anu Mahadevan\* and Raj K. Razdan



**Validation of an automated procedure for the prediction of relative free energies of binding on a set of aldose reductase inhibitors**

pp 7865–7877

Anna Maria Ferrari, Gianluca Degliesposti, Miriam Sgobba and Giulio Rastelli\*

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p I

\*Corresponding author

i\* Supplementary data available via ScienceDirect

**COVER**

Computational procedure for the prediction of relative free energies of binding. The structure of aldose reductase, the test-case enzyme used for validating the procedure, is shown as ribbon diagrams in the upper-left (holoenzyme) and lower (complex with a ligand) side of the figure. The procedure is able to screen automatically and iteratively molecules contained in databases (exemplified by the ensemble of 3D chemical structures in the upper-right corner) of compounds. Ranking and compound selection is based on binding free energy computation with molecular mechanics Poisson-Boltzmann surface area method (central part of the figure) [Ferrari, A. M.; Degliesposti, G.; Sgobba, M.; Rastelli, G. *Bioorg. Med. Chem.* **2007**, *15*, 7865–7877].

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