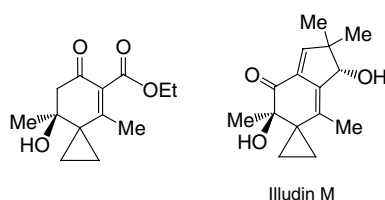


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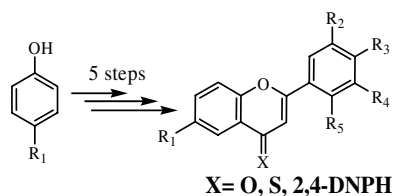
- Synthesis, reactions and structure–activity relationships of 1-hydroxyspiro[2.5]cyclooct-4-en-3-ones: Illudin analogs with in vitro cytotoxic activity** pp 4694–4703

Gopal Bose, Karin Bracht, Patrick J. Bednarski, Michael Lalk* and Peter Langer*



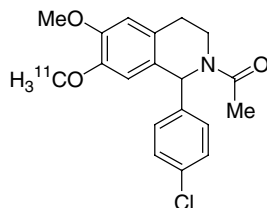
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- Closing in on the AMPA receptor: Synthesis and evaluation of 2-acetyl-1-(4'-chlorophenyl)-6-methoxy-7-[¹¹C]methoxy-1,2,3,4-tetrahydroisoquinoline as a potential PET tracer** pp 4712–4717

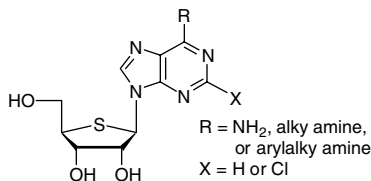
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Design, synthesis, and biological activity of *N*⁶-substituted-4'-thioadenosines at the human A₃ adenosine receptor

pp 4718–4730

Lak Shin Jeong,* Hyuk Woo Lee, Hea Ok Kim, Ji Young Jung, Zhan-Guo Gao, Heng T. Duong, Srikar Rao, Kenneth A. Jacobson, Dae Hong Shin, Jeong A Lee, Prashantha Gunaga, Sang Kook Lee, Dong Zhe Jin, Moon Woo Chun and Hyung Ryong Moon



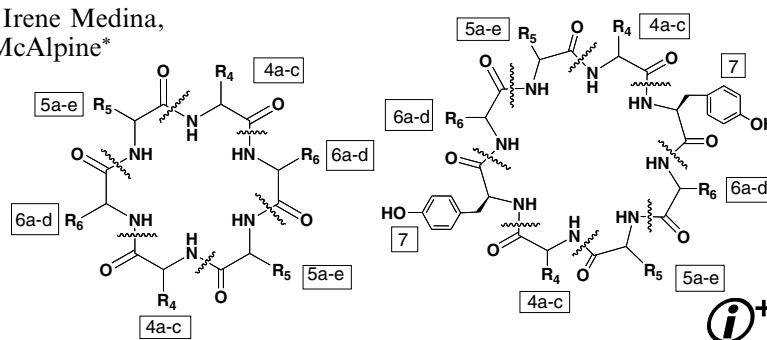
Structure–activity relationship of *N*⁶-substituted-4'-thioadenosines as potent human A₃ adenosine receptor agonists is described.

Novel antibiotics: C-2 symmetrical macrocycles inhibiting Holliday junction DNA binding by *E. coli* RuvC

pp 4731–4739

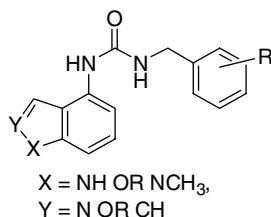
Po-Shen Pan, Fiona A. Curtis, Chris L. Carroll, Irene Medina, Lisa A. Liotta, Gary J. Sharples* and Shelli R. McAlpine*

Macrocyclic hexa- and octapeptides designed to trap Holliday junctions


Structure–activity studies of a novel series of 5,6-fused heteroaromatic ureas as TRPV1 antagonists

pp 4740–4749

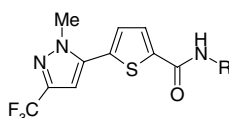
Irene Drizin,* Arthur Gomtsyan, Erol K. Bayburt, Robert G. Schmidt, Guo Zhu Zheng, Richard J. Perner, Stanley DiDomenico, John R. Koenig, Sean C. Turner, Tammie K. Jinkerson, Brian S. Brown, Ryan G. Keddy, Heath A. McDonald, Prisca Honore, Carol T. Wismer, Kennan C. Marsh, Jill M. Wetter, James S. Polakowski, Jason A. Segreti, Michael F. Jarvis, Connie R. Faltynek and Chih-Hung Lee


Novel potent and selective calcium-release-activated calcium (CRAC) channel inhibitors.

pp 4750–4760

Part 1: Synthesis and inhibitory activity of 5-(1-methyl-3-trifluoromethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamides

Yasuhiro Yonetoku,* Hirokazu Kubota, Yoshinori Okamoto, Akira Toyoshima, Masashi Funatsu, Jun Ishikawa, Makoto Takeuchi, Mitsuaki Ohta and Shin-ichi Tsukamoto

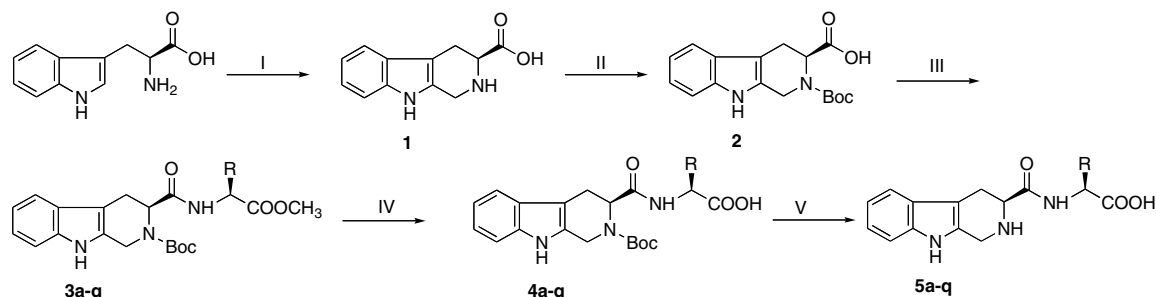


5-(1-Methyl-3-trifluoromethyl-1*H*-pyrazol-5-yl)thiophene-2-carboxamide derivatives were prepared and evaluated for their CRAC channel inhibitory activity.

Synthesis of new class dipeptide analogues with improved permeability and antithrombotic activity

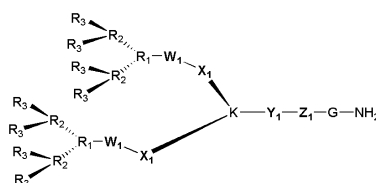
pp 4761–4774

Ming Zhao, Lanrong Bi, Wei Bi, Chao Wang, Zhe Yang, Jingfang Ju* and Shiqi Peng*

**Synthesis of a library of polycationic lipid core dendrimers and their evaluation in the delivery of an oligonucleotide with hVEGF inhibition**

pp 4775–4780

Harendra S. Parekh,* Robert J. Marano, Elizabeth P. Rakoczy, Joanne Blanchfield and Istvan Toth

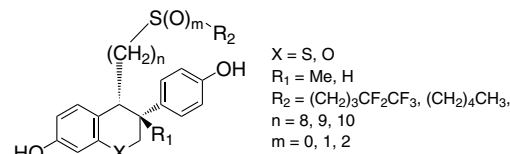


Discovery of thiochroman and chroman derivatives as pure antiestrogens and their structure–activity relationship

pp 4803–4819

Yoshitake Kanbe,* Myung-Hwa Kim, Masahiro Nishimoto, Yoshihito Ohtake, Nobuaki Kato, Toshiaki Tsunenari, Kenji Taniguchi, Iwao Ohizumi, Shin-ichi Kaiho, Kazumi Morikawa, Jae-Chon Jo, Hyun-Suk Lim and Hak-Yeop Kim

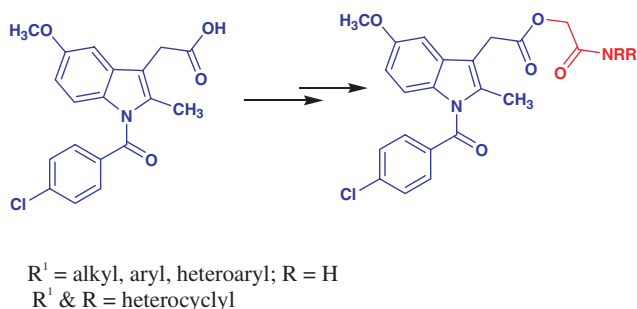
In order to develop pure antiestrogens, a series of 7-hydroxy-3-(4-hydroxyphenyl)chroman and 7-hydroxy-3-(4-hydroxyphenyl)thiochroman derivatives with sulfoxide containing side chains at the 4-position were designed, synthesized, and evaluated.



Evaluation of glycolamide esters of indomethacin as potential cyclooxygenase-2 (COX-2) inhibitors

pp 4820–4833

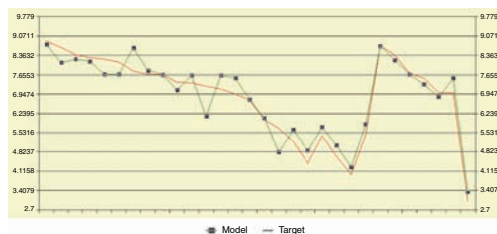
Smriti Khanna, Manjula Madan, Akhila Vangoori, Rahul Banerjee, Ram Thaimattam, S.K. Jafar Sadik Basha, Mullangi Ramesh, Seshagiri Rao Casturi and Manojit Pal*



QSAR study of 1,4-dihydropyridine calcium channel antagonists based on gene expression programming

pp 4834–4841

Hong Zong Si,* Tao Wang, Ke Jun Zhang, Zhi De Hu* and Bo Tao Fan



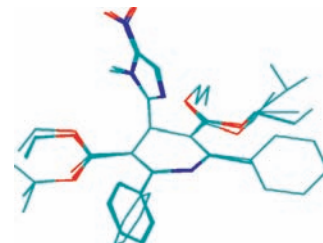
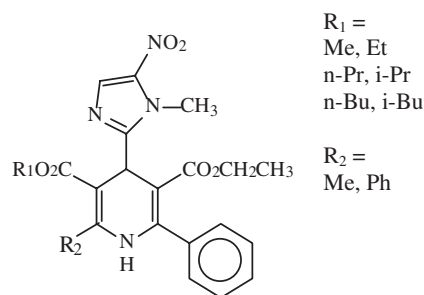
The log(1/IC₅₀) for 45 1,4-dihydropyridines was modeled using the descriptors calculated from the molecular structure along with a quantitative structure–activity relationship (QSAR) technique. The heuristic method (HM) and gene expression programming (GEP) were utilized to construct the linear and nonlinear prediction models, leading to a good prediction.

Synthesis, study of 3D structures, and pharmacological activities of lipophilic nitroimidazolyl-1,4-dihydropyridines as calcium channel antagonist

pp 4842–4849

Ramin Miri,* Katayoun Javidnia, Hasti Sarkarzadeh and Bahram Hemmateenejad*

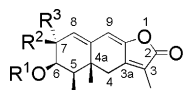
A group of alkyl ester analogues of new derivatives of nifedipine, in which the ortho-nitrophenyl group at position 4 is replaced by a 1-methyl-5-nitro-2-imidazolyl substituent, and the methyl group at position 6 is replaced by a phenyl substituent, were synthesized and evaluated as calcium channel antagonist using the high K⁺ contraction of guinea-pig ileal longitudinal smooth muscle.



Nonsteroidal progesterone receptor ligands (I): Synthesis and SAR of new tetrahydronaphthofuranone derivatives

pp 4850–4861

Rie Shinei,* Ken-ichi Kurihara, Kiyoshi Tanabe, Yuji Tabata, Yasushi Kurata, Shigeru Hoshiko and Tsuneo Okonogi

**PF1092C:** R¹ = H, R² = OH, R³ = H**8b:** R¹ = EtCO, R² = EtCOO, R³ = H**19i:** R¹ = cyclopropyl-NHCO, R² = H, R³ = MeO

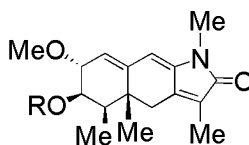
Tetrahydronaphthofuranones, based on the fungal metabolite PF1092C, was synthesized and evaluated for progesterone receptor (PR) binding affinities. Compounds **8b** and **19i** exhibited high affinity and acted as selective PR antagonists.

Nonsteroidal progesterone receptor ligands (II); synthesis and SAR of new tetrahydrobenzindolone derivatives

pp 4862–4878

Ken-ichi Kurihara,* Rie Shinei, Kiyoshi Tanabe, Yuji Tabata, Yasushi Kurata, Shigeru Hoshiko and Tsuneo Okonogi

We have developed a new lead compound, tetrahydrobenzindolone, possessing a lactam ring, which shows sufficient stability for easy modification at the 6- and/or 7-positions. We succeeded in separating the agonistic and antagonistic activities by choosing suitable substituent groups at the 6- and/or 7-position(s) of the tetrahydrobenzindolone.

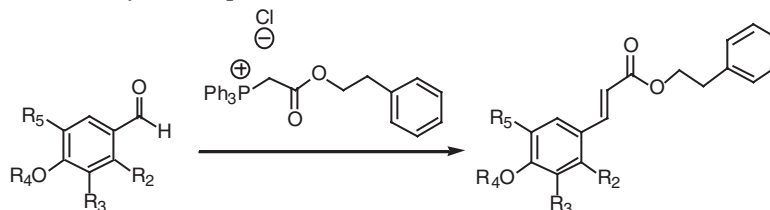


tetrahydrobenzindolone deriv.

PR agonist: R = *n*-PrNHCOR = Me₂NCOPR antagonist: R = (CH₃)₂CH(CH₂)₂-**Cytoprotective effect of caffeic acid phenethyl ester (CAPE) and catechol ring-fluorinated CAPE derivatives against menadione-induced oxidative stress in human endothelial cells**

pp 4879–4887

Xinyu Wang, Salomon Stavchansky,* Phillip D. Bowman and Sean M. Kerwin*



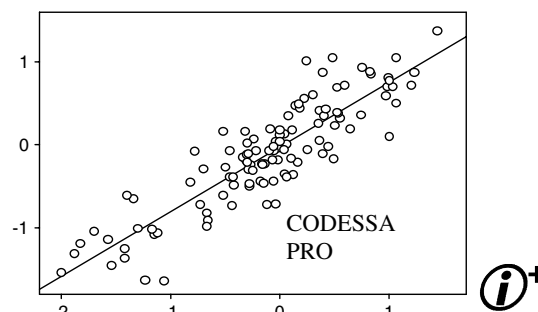
R₂ = H, **F**
 R₃ = H, OH, OMe
 R₄ = H, Me
 R₅ = **F**, OH, OMe

Correlation of blood–brain penetration using structural descriptors

pp 4888–4917

Alan R. Katritzky,* Minati Kuanar, Svetoslav Slavov, Dimitar A. Dobchev, Dan C. Fara, Mati Karelson, William E. Acree Jr., Vitaly P. Solov'ev and Alexandre Varnek

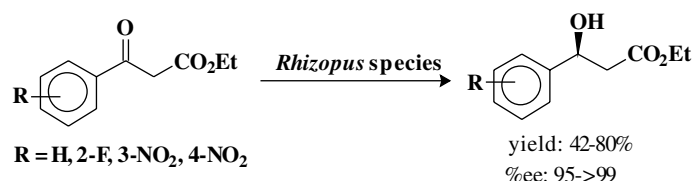
QSAR models of log BB for a diverse set of 113 drug molecules were developed employing structural descriptors using CODESSA-PRO and ISIDA approaches. The models were successfully validated using the central nervous system activity data of an external test set of 40 drug molecules.



Asymmetric reduction of 3-aryl-3-keto esters using *Rhizopus* species

pp 4918–4922

Neeta A. Salvi and Subrata Chattopadhyay*

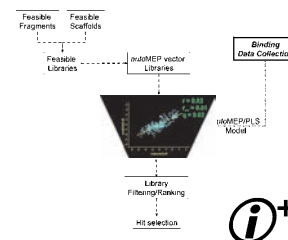


The application of a 3D-QSAR (*auto*MEP/PLS) approach as an efficient pharmacodynamic-driven filtering method for small-sized virtual library: Application to a lead optimization of a human A₃ adenosine receptor antagonist

pp 4923–4932

Stefano Moro,* Magdalena Bacilieri, Barbara Cacciari, Chiara Bolcato, Claudia Cusan, Giorgia Pastorin, Karl-Norbert Klotz and Giampiero Spalluto*

We present the application of 3D-QSAR (*auto*MEP/PLS) approach as an efficient and alternative pharmacodynamic filtering method for small-sized virtual library. For this purpose, a small-sized combinatorial library (841 compounds) was derived from the scaffold of the known human A₃ antagonist pyrazolo-triazolo-pyrimidines.

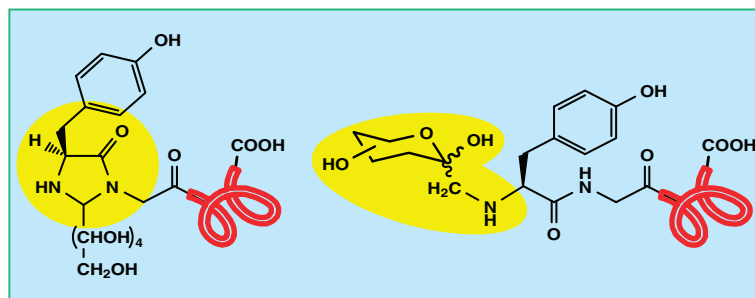


Transformations of bioactive peptides in the presence of sugars—Characterization and stability studies of the adducts generated via the Maillard reaction

pp 4933–4943

Maja Rošćić and Štefica Horvat*

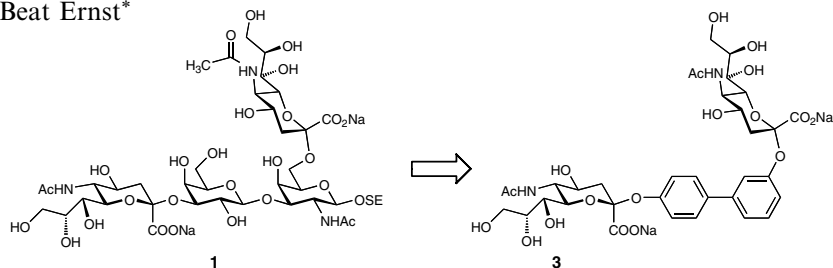
Glycation—a sweet hazard. Mechanism of formation in correlation with analysis in human serum improved our understanding of the underlying chemistry in the Maillard reaction.



Antagonists of the myelin-associated glycoprotein: A new class of tetrasaccharide mimics

pp 4944–4957

Daniel Schwizer, Heiko Gäthje, Soerge Kelm, Michele Porro, Oliver Schwardt and Beat Ernst*



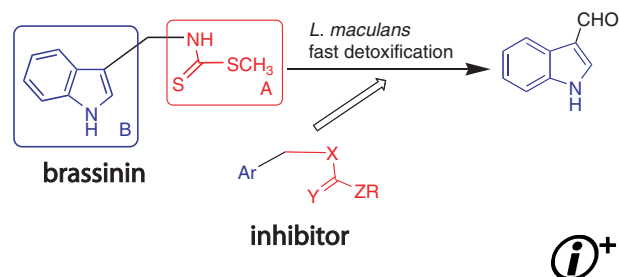
Simplified mimics of tetrasaccharide **1**, where the core disaccharide Galβ(1-3)GalNAc was replaced with a biphenyl, were synthesized and biologically evaluated as inhibitors of the myelin-associated glycoprotein (MAG).

Toward the control of *Leptosphaeria maculans*: Design, syntheses, biological activity, and metabolism of potential detoxification inhibitors of the crucifer phytoalexin brassinin

pp 4958–4979

M. Soledade C. Pedras* and Mukund Jha

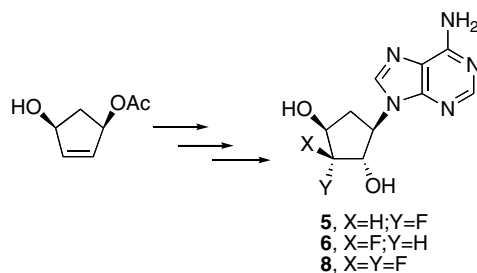
Potential inhibitors of brassinin detoxification were designed by replacement of the moiety A with carbamate, dithiocarbonate, urea, thiourea, sulfamide, sulfonamide, dithiocarbamate, amide, and ester groups, and moiety B with naphthalenyl and phenyl.



3'-Fluoro-3'-deoxy-5'-noraristeromycin derivatives: Synthesis and antiviral analysis

pp 4980–4986

Atanu Roy, Tesfaye Serbessa and Stewart W. Schneller*

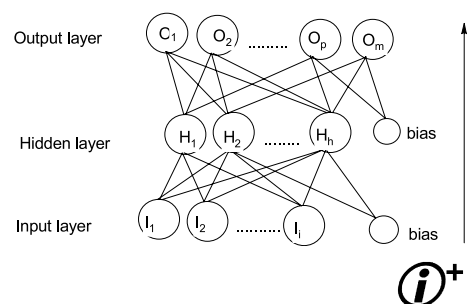


QSAR modeling of the inhibition of Glycogen Synthase Kinase-3

pp 4987–5002

Alan R. Katritzky,* Liliana M. Pacureanu, Dimitar A. Dobchev, Dan C. Fara, Pablo R. Duchowicz and Mati Karelson

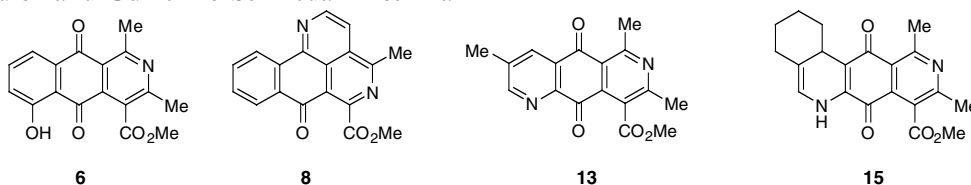
QSAR modeling of the biological activity (pIC_{50}) of 277 inhibitors of GSK-3 is developed using linear (multilinear regression) and nonlinear (artificial neural network) models. The results gave an insight into the dominant role played by the electrostatic, bonding, and steric interactions on the modulation of inhibitory activity.



Studies on quinones. Part 41: Synthesis and cytotoxicity of isoquinoline-containing polycyclic quinones

pp 5003–5011

Jaime A. Valderrama,* M. Florencia González, David Pessoa-Mahana, Ricardo A. Tapia, Houda Fillion, Felix Pautet, Jaime A. Rodriguez, Cristina Theoduloz and Guillermo Schmeda-Hirschmann

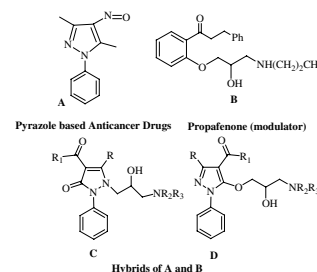


The regioselective synthesis of fused isoquinolinequinones (i.e., **6**, **8**, **13**, and **15**) through highly regiocontrolled cycloaddition reactions from methyl 1,3-dimethyl-5,8-dioxo-5,8-dihydroisoquinoline-4-carboxylate **3** and 1,3-dienes is reported. The 2-aza- and 1,6-diaza-anthraquinone derivatives displayed significant in vitro activity on normal fibroblast and four tumor cell lines.

Synthesis of pyrazole-based hybrid molecules: Search for potent multidrug resistance modulators**pp 5061–5071**

Palwinder Singh,* Kamaldeep Paul and Wolfgang Holzer

The hybrid molecules **C** and **D** obtained by combining the structural features of pyrazole-based drugs (**A**) and propafenone (a modulator) (**B**) have been synthesized and evaluated for their interactions with P-glycoprotein.

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*Corresponding author

①⁺ Supplementary data available via ScienceDirect**COVER**

The figure shows the synthetic approach to 6*RS* CB300945; an inhibitor of thymidylate synthase targeted at α -folate receptor overexpressing tumours. This compound and related derivatives were synthesised via multistep routes [Henderson, E.A.; Bavetsias, V.; Theti, D.S.; Wilson, S.C.; Clauss, R.; Jackman, A.L. *Bioorg. Med. Chem.* **2006**, *14*, 5020].



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