



Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry Letters

journal homepage: www.elsevier.com/locate/bmcl



Bioorganic & Medicinal Chemistry Letters Volume 20, Issue 13, 2010

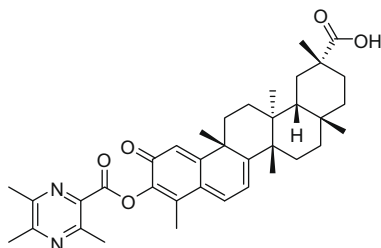
Contents

ARTICLES

Synthesis and preliminary evaluation of neuroprotection of celastrol analogues in PC12 cells

pp 3844–3847

Hongli Sun, Lipeng Xu*, Pei Yu, Jie Jiang, Gaoxiao Zhang, Yuqiang Wang*



CL12

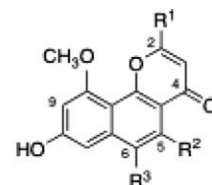
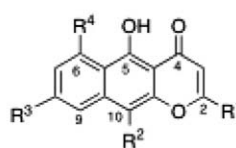


Inhibition of ABCG2-mediated drug efflux by naphthopyrones from marine crinoids

pp 3848–3850

Heidi R. Bokesch, Laura K. Cartner, Richard W. Fuller, Jennifer A. Wilson, Curtis J. Henrich, James A. Kelley, Kirk R. Gustafson, James B. McMahon, Tawnya C. McKee*

Five new naphthopyrones were isolated from marine crinoids as part of a screen looking for inhibitors of ABCG2-mediated efflux. Six known metabolites were isolated with the new compounds. Only the angular naphthopyrones were active against ABCG2-mediated efflux.



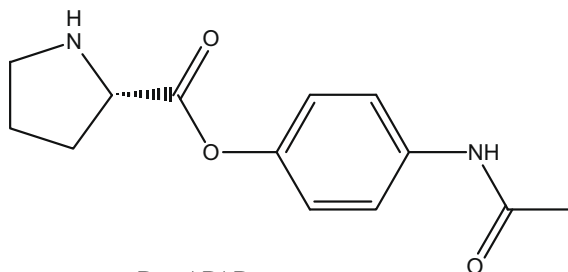
1: $R^1=CH_3$, $R^2=R^3=OCH_3$, $R^4=OH$
2: $R^1=CH_2CH_2CH_3$, $R^2=R^3=OCH_3$, $R^4=OH$

3: $R^1=CH_3$, $R^2=OH$, $R^3=OCH_3$
4: $R^1=CH_3$, $R^2=R^3=OCH_3$
5: $R^1=CH_2CH_2CH_3$, $R^2=OCH_3$, $R^3=H$

Development of acetaminophen proline prodrug

pp 3851–3854

Zhiqian Wu*, Ashish Patel, Rutesh Dave, Xudong Yuan

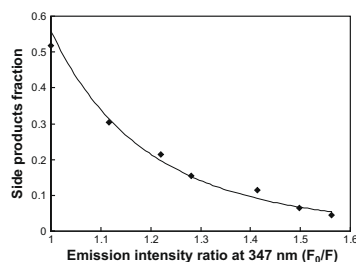


Pro-APAP

Structural change of the enterobactin synthetase in crowded solution and its relation to crowding-enhanced product specificity in nonribosomal enterobactin biosynthesis

pp 3855–3858

Zu-Feng Guo, Ming Jiang, Suilan Zheng, Zhihong Guo*



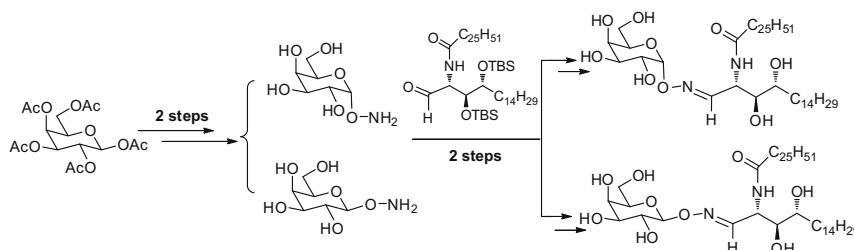
Macromolecular crowding is found to change the structure of the nonribosomal enterobactin synthetase to increase its product specificity.

Efficient synthesis of galactosylceramide analogues for iNKT cell stimulation

pp 3859–3862

Wenlan Chen, Chengfeng Xia, Li Cai, Peng George Wang*

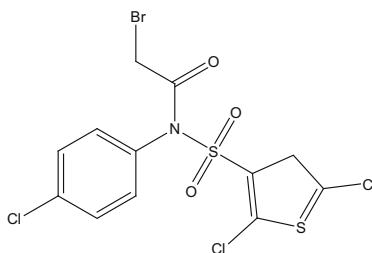
Glycolipids are potential antigens for iNKT cells recognition and demonstrate important roles in both innate and adaptive immunity. However, the difficulties in the preparation of pure configuration defined glycolipids limit the exploration of their different profiles in activating iNKT cells. We report here a concise and stereospecific preparation of novel galactosylceramide analogues by oxime ligation. This strategy would provide an efficient way to generate varied glycolipid analogues with either synthetic or natural carbohydrates for biological evaluations.



Activity of substituted thiophene sulfonamides against malarial and mammalian cyclin dependent protein kinases

pp 3863–3867

Diana Caridha, April K. Kathcart, Dayadevi Jirage, Norman C. Waters*



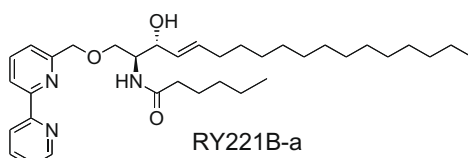
Various substituted thiophene and benzyl sulfonamides were identified as inhibitors of the plasmodial CDK, Pfmrk. Bromohydrosulfonylacetamides were selective for Pfmrk over human CDKs.



Synthesis and evaluation of novel phosphate ester analogs as neutral sphingomyelinase inhibitors

pp 3868–3871

Hiroshi Imagawa*, Masataka Oda, Takayuki Takemoto, Rieko Yamauchi, Tomomi Yoshikawa, Hirofumi Yamamoto, Mugio Nishizawa*, Hironobu Takahashi, Manabu Hashimoto, Kenta Yabiku, Masahiro Nagahama, Jun Sakurai*



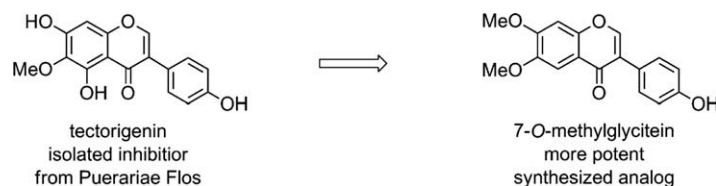
Neutral Sphingomyelinase Inhibitor ($IC_{50} = 1.2 \mu M$)



Inhibitors for expression of IgE receptor on human mast cell from Puerariae Flos

pp 3872–3875

Satoru Tamura, Kunichika Yoshihira, Mariko Tokumaru, Xu Zisheng, Nobutoshi Murakami*

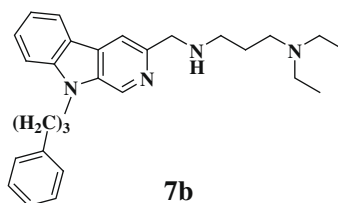


Tectorigenin was disclosed as the inhibitor for expression of IgE receptor on human mast cells from the medicinal plant, Puerariae Flos. Furthermore, survey for synthesized analogs brought about more potent 7-O-methyl glycitein.

Synthesis of novel β -carbolines with efficient DNA-binding capacity and potent cytotoxicity

pp 3876–3879

Zhiyong Chen, Rihui Cao*, Buxi Shi, Wei Yi, Liang Yu, Huacan Song*, Zhenhua Ren, Wenlie Peng

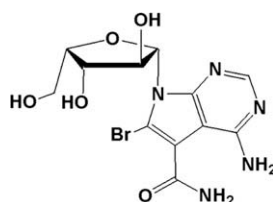


A series of water-soluble β -carbolines, bearing a flexible amino side chain, has been prepared and evaluated in vitro against a panel of human cell lines. Compound **7b** were found to be the most potent compound with IC_{50} values lower than 10 μ M against eight human tumor cell lines.

Cell cycle arrest and cytochrome c-mediated apoptotic induction by MCS-5A is associated with up-regulation of p16^{INK4a} in HL-60 cells

pp 3880–3884

Bu Young Choi, Chul-Hoon Lee*

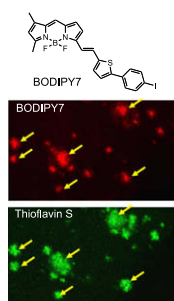


The chemical structure of MCS-5A 4-amino-6-bromo-7-(β -L-xylofuranosyl)pyrrolo[2,3-d]pyrimidine-5-carboxamide.

Development of dual functional SPECT/fluorescent probes for imaging cerebral β -amyloid plaques

pp 3885–3888

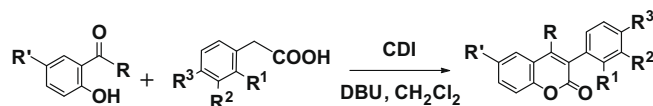
Masahiro Ono*, Manami Ishikawa, Hiroyuki Kimura, Shun Hayashi, Kenji Matsumura, Hiroyuki Watanabe, Yoichi Shimizu, Yan Cheng, Mengchao Cui, Hidekazu Kawashima, Hideo Saji*



A novel synthesis of 3-aryl coumarins and evaluation of their antioxidant and lipoxygenase inhibitory activity

pp 3889–3892

Marina Roussaki, Christos A. Kontogiorgis, Dimitra Hadjipavlou-Litina, Stylianos Hamilakis*, Anastasia Detsi

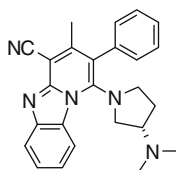


Novel 3-aryl-coumarin derivatives have been synthesized via a new methodology. The in vitro antioxidant and soybean lipoxygenase inhibitory activity of the new compounds has been evaluated.

Novel pyridobenzimidazole derivatives exhibiting antifungal activity by the inhibition of β -1,6-glucan synthesis

pp 3893–3896

Hiroshi Takeshita*, Jun Watanabe, Yoichi Kimura, Katsuhiro Kawakami, Hisashi Takahashi, Makoto Takemura, Akihiro Kitamura, Kazuhiko Someya, Ryohei Nakajima



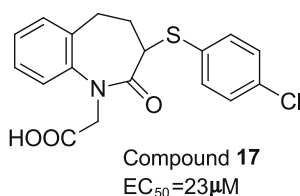
We have discovered novel pyridobenzimidazole derivatives, which exhibit antifungal activity by the inhibition of β -1,6-glucan synthesis.



Design and synthesis of benzoazepin-2-one analogs as allosteric binders targeting the PIF pocket of PDK1

pp 3897–3902

Linyi Wei, Xiaoqi Gao, Robert Warne, Xueshi Hao, Dirksen Bussiere, Xiang-ju Gu, Tetsuo Uno*, Yi Liu*

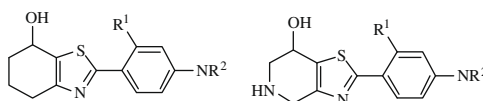


Design, synthesis and SARs of novel series of 2-thio-benzoazepin-2-one analogs as allosteric activators of PDK1 targeting the PIF pocket are reported.

2-Aryl-4,5,6,7-tetrahydro-1,3-benzothiazol-7-ols as a class of antitumor agents selectively active in securin^{-/-} cells

pp 3903–3905

Nan Zhang*, Semiramis Ayral-Kaloustian*, Chuansheng Niu, Thai Nguyen, Erik Upeslakis, Tarek S. Mansour, Shoba Rangunathan, Edward Rosfjord

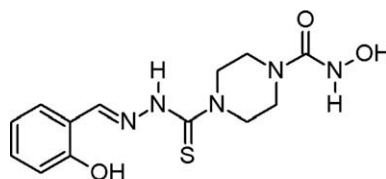


A series of 2-(4-aminophenyl)-4,5,6,7-tetrahydro-1,3-benzothiazol-7-ols and their 5-aza analogs, 2-(4-aminophenyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-c]pyridin-7-ols, demonstrated high levels of selectivity against aneuploid cell growth (vs diploid cells).

Design, synthesis and anticancer activity of piperazine hydroxamates and their histone deacetylase (HDAC) inhibitory activity

pp 3906–3910

Bhadaliya Chetan, Mahesh Bunha, Monika Jagrat, Barij Nayan Sinha, Philipp Saiko, Geraldine Graser, Thomas Szekeres, Ganapathy Raman, Praveen Rajendran, Dhatchana Moorthy, Arijit Basu, Venkatesan Jayaprakash*

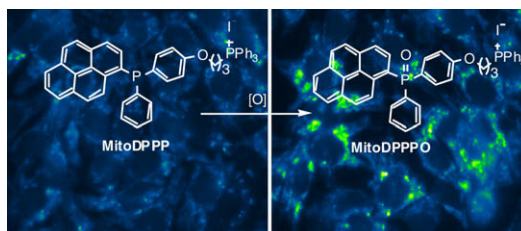
**5c**

Compound **5c** has shown mean GI_{50} : $9.33 \pm 1.3 \mu\text{M}$ against NCIH460, HCT116 and U251 cell lines and IC_{50} : $33.67 \mu\text{M}$ against HDAC8. It also inhibited HL60 human promyelocytic leukemia cell line due to the presence of pharmacophoric features of RR inhibitor.

**Synthesis and properties of fluorescence probe for detection of peroxides in mitochondria**

pp 3911–3915

Kosei Shioji*, Yu Oyama, Kentaro Okuma, Hiroyuki Nakagawa

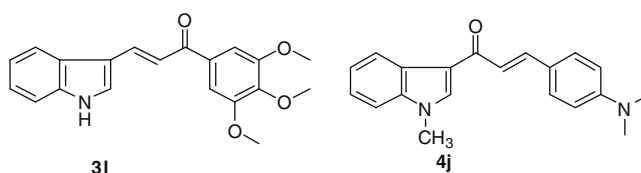


Diarylpyrenylphosphine-conjugated alkyltriphenylphosphonium was accumulated in mitochondria, and it detected the penetration or generation of peroxide in a mitochondrial lipid bilayer.

**Synthesis and biological evaluation of indolyl chalcones as antitumor agents**

pp 3916–3919

Dalip Kumar*, N. Maruthi Kumar, Kanako Akamatsu, Eriko Kusaka, Hiroshi Harada, Takeo Ito*

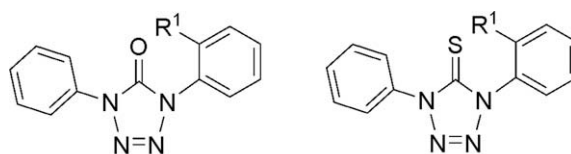


A series of indolyl chalcones were synthesized and evaluated for their in vitro anti-proliferative activities against various cancer cell lines.

Synthesis and antiproliferative evaluation of 5-oxo and 5-thio derivatives of 1,4-diaryl tetrazoles

pp 3920–3924

Aditya S. Gundugola, Kusum Lata Chandra, Elisabeth M. Perchellet, Andrew M. Waters, Jean-Pierre H. Perchellet, Sundeep Rayat*



$R^1 = \text{H, OMe, Cl, CF}_3, \text{Br, C}\equiv\text{CH, OH}$

We report the synthesis of a series of 1,4-diaryl tetrazol-5-ones and tetrazole-5-thiones that inhibit the proliferation of L1210 and SK-BR-3 tumor cells in vitro.

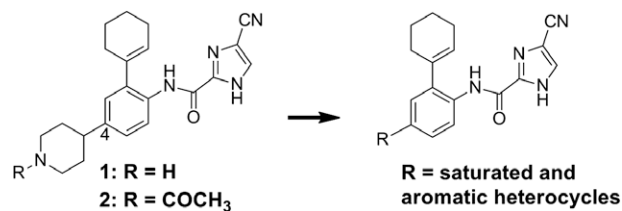


Reducing ion channel activity in a series of 4-heterocyclic arylamide FMS inhibitors

pp 3925–3929

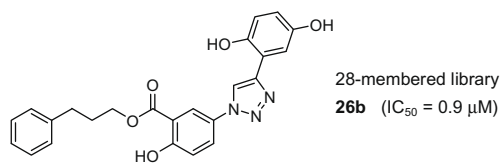
Kenneth J. Wilson*, Carl R. Illig, Jinsheng Chen, Mark J. Wall, Shelley K. Ballentine, Renee L. DesJarlais, Yanmin Chen, Carsten Schubert, Robert Donatelli, Ioanna Petrounia, Carl S. Crysler, Christopher J. Molloy, Margery A. Chaikin, Carl L. Manthey, Mark R. Player, Bruce E. Tomczuk, Sanath K. Meegalla

During efforts to improve the bioavailability of FMS kinase inhibitors **1** and **2**, a series of saturated and aromatic 4-heterocycles of reduced basicity were prepared and evaluated in an attempt to also improve the cardiovascular safety profile over lead arylamide **1**, which possessed ion channel activity. The resultant compounds retained excellent potency and exhibited diminished ion channel activity.

**A rapid synthesis of lavendustin-mimetic small molecules by click fragment assembly**

pp 3930–3935

Jieun Yoon, Jae-Sang Ryu*

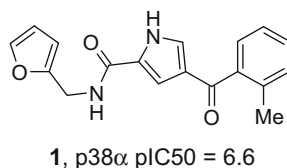


A lavendustin-mimetic small-molecule library has been synthesized via a click chemistry. 3-Phenylpropyl ester **26b** inhibited CCRF-CEM leukemia cell growth with GI₅₀ value of 0.9 μM.

**The discovery and initial optimisation of pyrrole-2-carboxamides as inhibitors of p38α MAP kinase**

pp 3936–3940

Kenneth Down*, Paul Bamborough*, Catherine Alder, Amanda Campbell, John A. Christopher, Maria Gerelle, Steve Ludbrook, Dave Mallett, Geoff Mellor, David D. Miller, Rosannah Pearson, Keith Ray, Yemisi Solanke, Don Somers

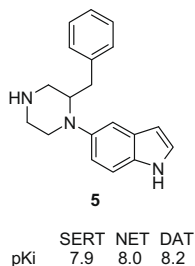


A novel pyrrole-2-carboxamide series of p38α inhibitors, discovered through the application of virtual screening, is presented.

2-Substituted N-aryl piperazines as novel triple reuptake inhibitors for the treatment of depression

pp 3941–3945

David S. Carter*, Hai-Ying Cai, Eun Kyung Lee, Pravin S. Iyer, Matthew C. Lucas, Ralf Roetz, Ryan C. Schoenfeld, Robert J. Weikert

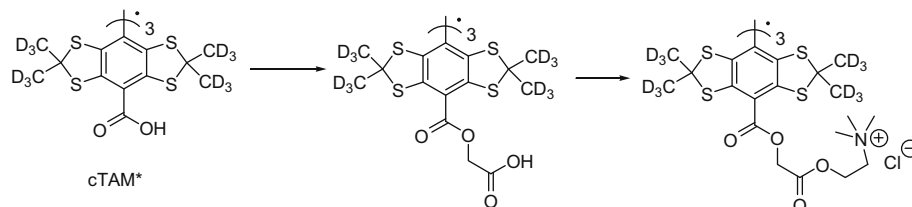


The discovery and optimization of a novel series of 2-substituted N-aryl piperazine based triple reuptake inhibitors is described.

Synthesis, structure, and EPR characterization of deuterated Finland trityl radical

pp 3946–3949

Ilirian Dhimitruka, Olga Grigorieva, Jay L. Zweier, Valery V. Khramtsov*

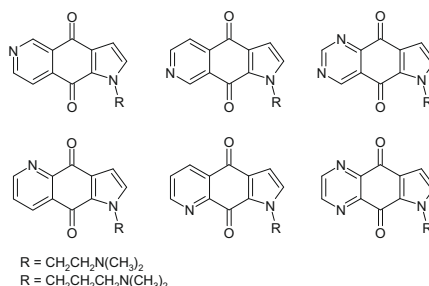


Substituted trityl radicals are important spin probes for functional electron paramagnetic resonance spectroscopy and imaging including oxygen and pH mapping in vivo. Here we report an efficient synthetic procedure for the synthesis of deuterated Finland trityl radical, cTAM*, and its derivatives. The effect of deuterio-substitution on EPR spectra of homologous derivatives has been evaluated. The compounds are potential candidates for targeted spin probes in EPR imaging and spectroscopy.

**Synthesis and biological evaluation of new cytotoxic azanaphthoquinone pyrrolo-annelated derivatives**

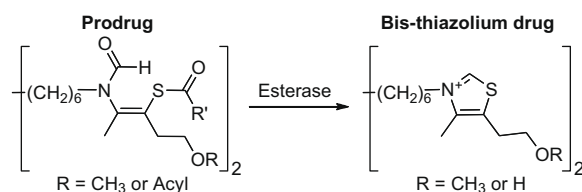
pp 3950–3952

Karem Shanab, Eva Schirmer, Heike Knafl, Eva Wulz, Wolfgang Holzer, Helmut Spreitzer*, Peter Schmidt, Babette Aicher, Gilbert Müller, Eckhard Günther

**Exploration of potential prodrug approach of the bis-thiazolium salts T3 and T4 for orally delivered antimalarials**

pp 3953–3956

Sergio A. Caldarelli, Michel Boisbrun, Karine Alarcon, Abdallah Hamzé, Mahama Ouattara, Xavier Salom-Roig, Marjorie Maynadier, Sharon Wein, Suzanne Peyrottes, Alain Pellet, Michèle Calas, Henri Vial*

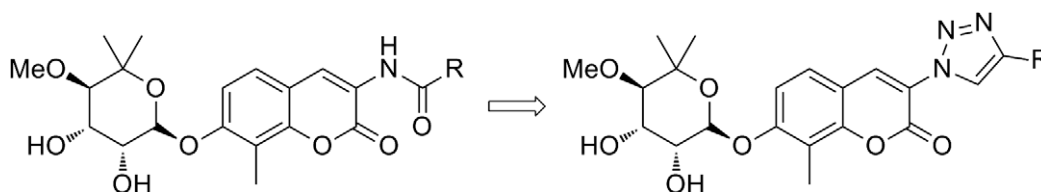


The synthesis and biological activities of a series of bis-thiazolium prodrugs are reported.

**Click chemistry to probe Hsp90: Synthesis and evaluation of a series of triazole-containing novobiocin analogues**

pp 3957–3960

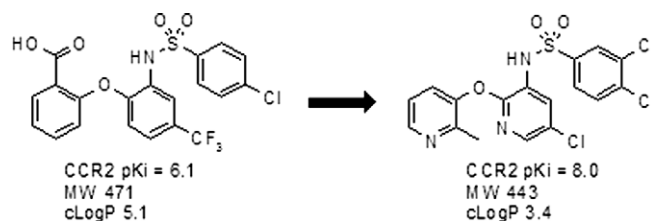
Laura B. Peterson, Brian S.J. Blagg*



Identification of a sulfonamide series of CCR2 antagonists

pp 3961–3964

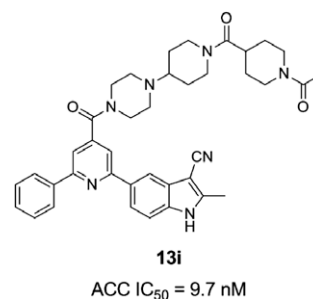
Simon Peace*, Joanne Philp, Carl Brooks, Val Piercy, Kitty Moores, Chris Smethurst, Steve Watson, Simon Gaines, Mara Zippoli, Claudette Mookherjee, Robert Ife

**Design and synthesis of disubstituted (4-piperidinyl)-piperazine derivatives as potent acetyl-CoA carboxylase inhibitors**

pp 3965–3968

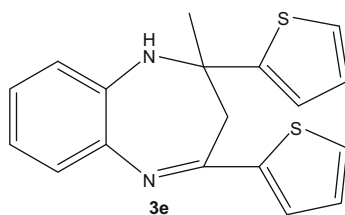
Tomomichi Chonan*, Hiroaki Tanaka, Daisuke Yamamoto, Miyoko Yashiro, Takahiro Oi, Daisuke Wakasugi, Ayumi Ohoka-Sugita, Fusayo Io, Hiroko Koretsune, Akira Hiratake

Novel unsymmetric disubstituted pyridines as ACC1/2 non-selective inhibitors were synthesized and evaluated.

**Anti-neuroinflammatory activity of 1,5-benzodiazepine derivatives**

pp 3969–3971

Sang Keun Ha, Donthabhaktuni Shobha, Eunjung Moon, Murugulla A. Chari, Kaggla Mukkanti, Sung-Hoon Kim, Kwang-Hyun Ahn*, Sun Yeou Kim*



1,5-Benzodiazepine derivatives such as compound **3e** showed a good anti-neuroinflammatory effects by suppressing iNOS enzyme activity in microglia cells.

Structure based design of novel inhibitors for histidinol dehydrogenase from *Geotrichum candidum*

pp 3972–3976

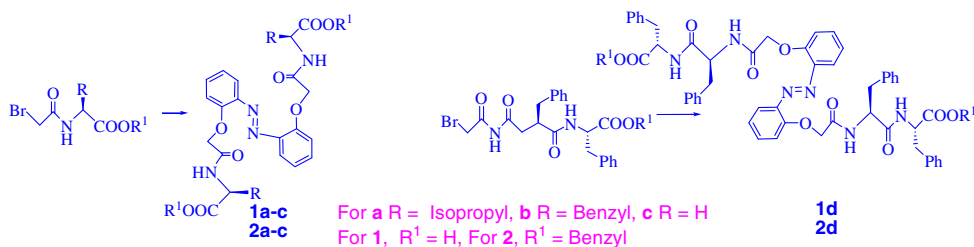
Sonia Pahwa, Simranjeet Kaur, Rahul Jain, Nilanjan Roy*



C₂-Symmetric azobenzene-amino acid conjugates and their inhibition of Subtilisin Kexin Isozyme-1

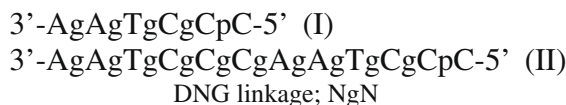
pp 3977–3981

Amit Basak*, Debarati Mitra, Amit K. Das, Dayani Mohottalage, Ajoy Basak*

The compounds (**1** and **2**) showed inhibition of SKI-1 in micromolar concentrations.**Development of potential anticancer agents that target the telomere sequence**

pp 3982–3986

Myunji Park, Thomas C. Bruice*



Oligonucleotides containing positively charged ribonucleic guanine linkages (DNG I, II) have been synthesized to develop anticancer agents targeting telomere. Binding properties of DNG I, II are presented.

*Corresponding author

Supplementary data available via ScienceDirect

COVER

Overlay of high resolution co-crystal structures of **R-22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, 17, 5677.]

Available online at www.sciencedirect.com

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE. Also covered in the abstract and citation database SCOPUS®. Full text available on ScienceDirect®



ELSEVIER

ISSN 0960-894X