Bioorganic & Medicinal Chemistry 20 (2012) 3687–3694

Contents lists available at SciVerse ScienceDirect

Bioorganic & Medicinal Chemistry

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

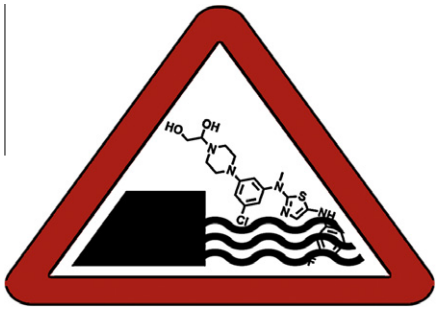
Bioorganic & Medicinal Chemistry Volume 20, Issue 12, 2012

Contents

PERSPECTIVE

Change or be changed. Reflections of the workshop 'Future in Medicinal Chemistry' **pp 3695–3697**

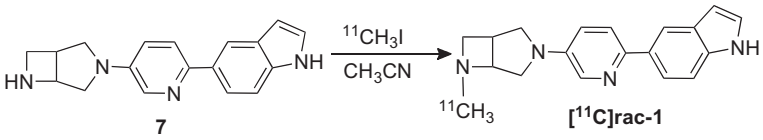
Ruth Brenk*, Daniel Rauh*



ARTICLES

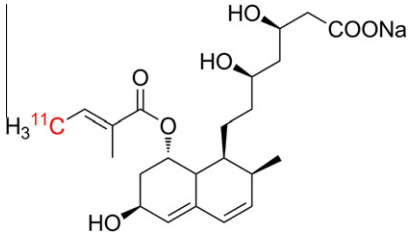
5-(5-(6-[^{11}C]methyl-3,6-diazabicyclo[3.2.0]heptan-3-yl)pyridin-2-yl)-1*H*-indole as a potential PET radioligand for imaging cerebral α7-nAChR in mice **pp 3698–3702**

Yongjun Gao*, Hayden T. Ravert, Heather Valentine, Ursula Scheffel, Paige Finley, Dean F. Wong, Robert F. Dannals, Andrew G. Horti



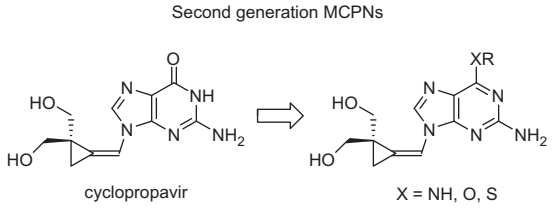
Synthesis of [^{11}C]dehydropravastatin, a PET probe potentially useful for studying OATP1B1 and MRP2 transporters in the liver **pp 3703–3709**

Ryosuke Ijuin, Tadayuki Takashima, Yasuyoshi Watanabe, Yuichi Sugiyama, Masaaki Suzuki*

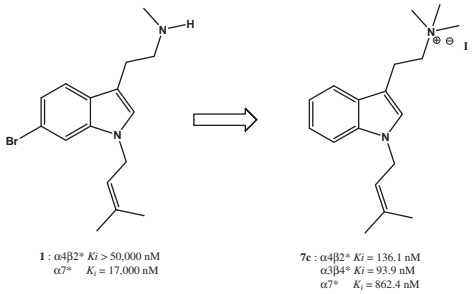


The synthesis of [^{11}C]2′,3′-dehydropravastatin has been accomplished by the rapid cross-coupling (*C*-[^{11}C]methylation reaction) between $sp^2_{(vinyl)}$-sp^3 carbons using [^{11}C]methyl iodide and an organoboron precursor in the ^{11}C-labeling step, and subsequent deprotection and hydrolysis.

Synthesis and antiviral activity of certain second generation methylenecyclopropane nucleosides **pp 3710–3718**
John D. Williams*, Atiyya R. Khan, Emma A. Harden, Caroll B. Hartline, Geraldine M. Jefferson, Kathy A. Keith, Mark N. Prichard, Jiri Zemlicka, Norton P. Peet, Terry L. Bowlin

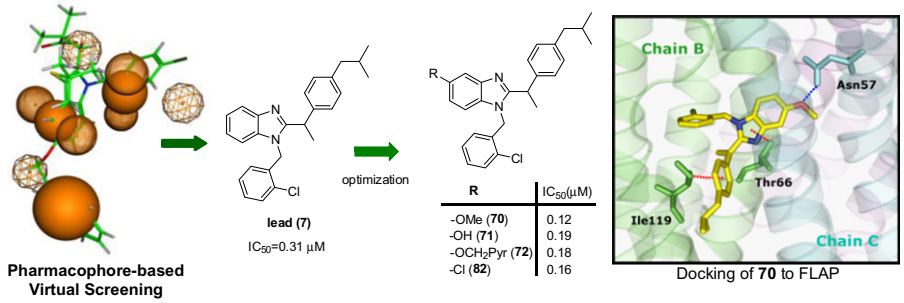


Synthesis and evaluation of N^1-alkylindole-3-ylalkylammonium compounds as nicotinic acetylcholine receptor ligands **pp 3719–3727**
Edwin G. Pérez*, Bruce K. Cassels, Christoph Eibl, Daniela Gündisch

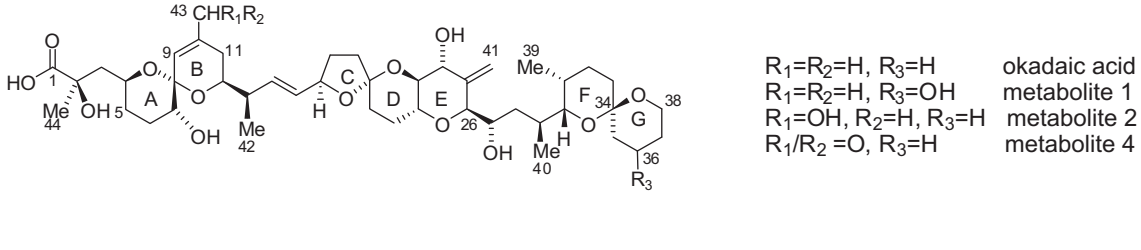


We report the synthesis and pharmacological evaluation of a series of new nicotinic acetylcholine receptor ligands. The new compounds were based on the structure of **1**, an alkaloid isolated from the marine bryozoan *Flustra foliacea* L.

Identification of novel benzimidazole derivatives as inhibitors of leukotriene biosynthesis by virtual screening targeting 5-lipoxygenase-activating protein (FLAP) **pp 3728–3741**
Erden Banoglu*, Burcu Çalışkan, Susann Luderer, Gökçen Eren, Yagmur Özkan, Wolfram Altenhofen, Christina Weinigel, Dagmar Barz, Jana Gerstmeier, Carlo Pergola, Oliver Werz*

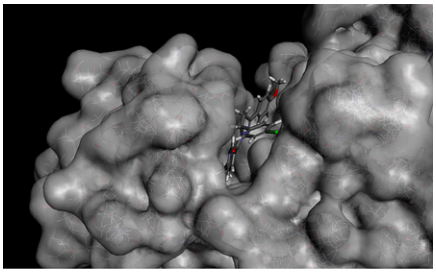


The structures of three metabolites of the algal hepatotoxin okadaic acid produced by oxidation with human cytochrome P450 **pp 3742–3745**
Li Liu, Fujiang Guo, Sheila Crain, Michael A. Quilliam, Xiaotang Wang, Kathleen S. Rein*



Synthesis, biological evaluation and 3D-QSAR studies of novel 4,5-dihydro-1*H*-pyrazole niacinamide derivatives as BRAF inhibitors **pp 3746–3755**

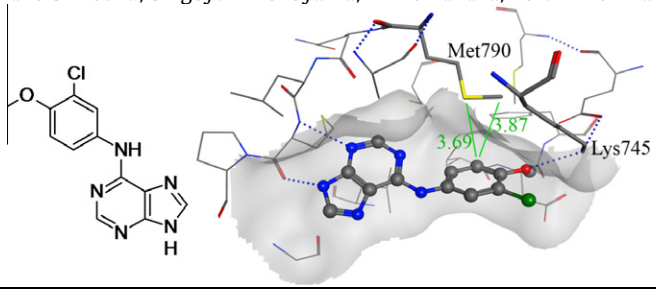
Cui-Yun Li, Qing-Shan Li, Li Yan, Xiao-Guang Sun, Ran Wei, Hai-Bin Gong*, Hai-Liang Zhu*



A new series of novel 4,5-dihydropyrazole derivatives containing niacinamide moiety were designed, synthesized and evaluated for biological activities as potential V600E mutant BRAF kinase ($BRAF^{V600E}$) inhibitors. Among these compounds, **27e** ((5-(4-Chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)6-methylpyridin-3-yl methanone) showed the most potent agent against BRAF and WM266.4 human melanoma cell line with IC_{50} value of 0.20 μM and GI_{50} value of 0.89 μM. Docking simulation was performed to insert compound **27e** into the crystal structure of BRAF to determine the probable binding model. QSAR model was also built to provide a reliable tool for rational design of novel BRAF inhibitors.

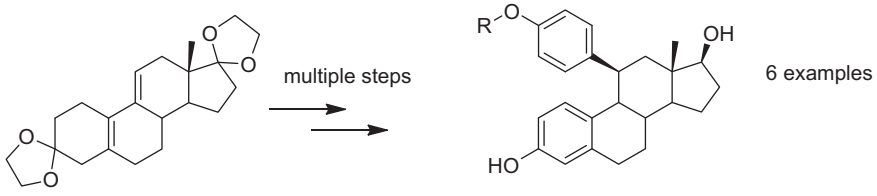
Identification of novel drug-resistant EGFR mutant inhibitors by in silico screening using comprehensive assessments of protein structures **pp 3756–3767**

Tomohiro Sato, Hisami Watanabe, Keiko Tsuganezawa, Hitomi Yuki, Junko Mikuni, Seiko Yoshikawa, Mutsuko Kukimoto-Niino, Takako Fujimoto, Yumiko Terazawa, Motoaki Wakiyama, Hirotatsu Kojima, Takayoshi Okabe, Tetsuo Nagano, Mikako Shirouzu, Shigeyuki Yokoyama, Akiko Tanaka, Teruki Honma*



Synthesis and evaluation of 11β-(4-Substituted phenyl) estradiol analogs: Transition from estrogen receptor agonists to antagonists **pp 3768–3780**

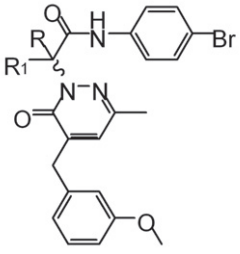
Robert N. Hanson*, Edward Hua, J. Adam Hendricks, David Labaree, Richard B. Hochberg



R groups transition from ER agonists to ER antagonists

Synthesis, enantioresolution, and activity profile of chiral 6-methyl-2,4-disubstituted pyridazin-3(2*H*)-ones as potent *N*-formyl peptide receptor agonists **pp 3781–3792**

Agostino Cilibrizzi, Igor A. Schepetkin, Gianluca Bartolucci, Letizia Crocetti, Vittorio Dal Piaz, Maria Paola Giovannoni*, Alessia Graziano, Liliya N. Kirpotina, Mark T. Quinn, Claudia Vergelli

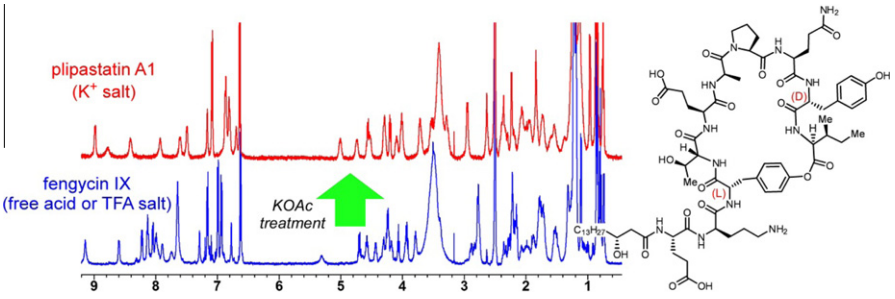


R = CH_3, C_2H_5, n-C_3H_7, i-C_3H_7, n-C_4H_9, C_6H_5
R_1 = H, CH_3

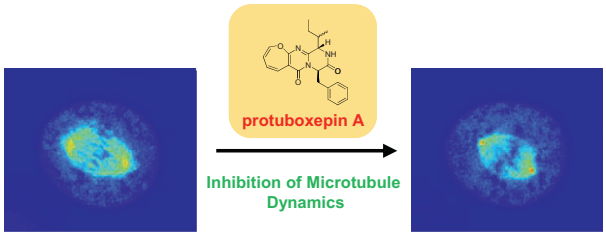
R-(-)-5e (R=H, R_1= n-C_4H_9)

FPR1 IC_{50}=0.5 μM
FPR2 IC_{50}=0.089 μM

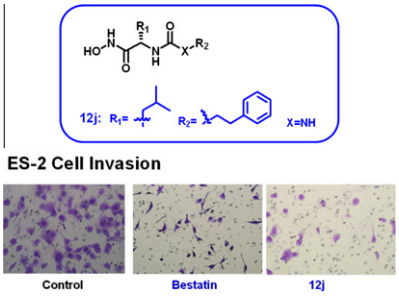
Termination of the structural confusion between plipastatin A1 and fengycin IX **pp 3793–3798**
Miho Honma, Kazuaki Tanaka, Katsuhiro Konno, Kenji Tsuge, Toshikatsu Okuno, Masaru Hashimoto*



Protuboxepin A, a marine fungal metabolite, inducing metaphase arrest and chromosomal misalignment in tumor cells **pp 3799–3806**
Yukihiro Asami, Jae-Hyuk Jang, Nak-Kyun Soung, Long He, Dong Oh Moon, Jong Won Kim, Hyuncheol Oh, Makoto Muroi, Hiroyuki Osada, Bo Yeon Kim*, Jong Seog Ahn*

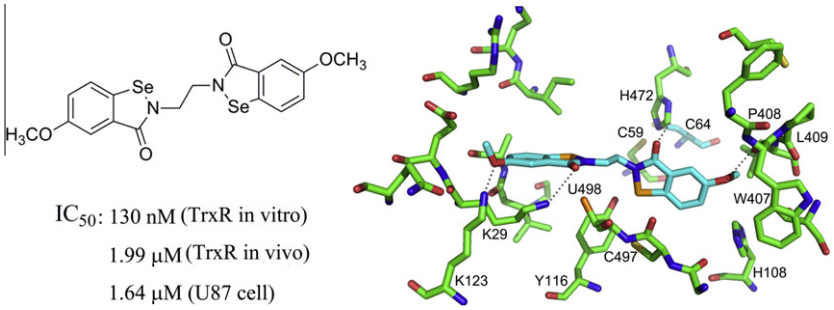


Design, synthesis and biological evaluation of novel amino acid ureido derivatives as aminopeptidase N/CD13 inhibitors **pp 3807–3815**
Li Su, Yuping Jia, Lei Zhang, Yingying Xu, Hao Fang, Wenfang Xu*

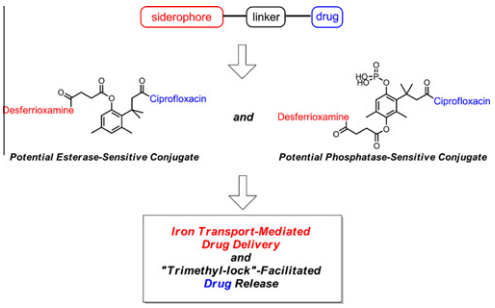


Graphical abstractNovel amino acid ureido derivatives were achieved as APN inhibitors, among which **12j** exhibited more potent anti-proliferation and anti-invasion effects than Bestatin on the market.

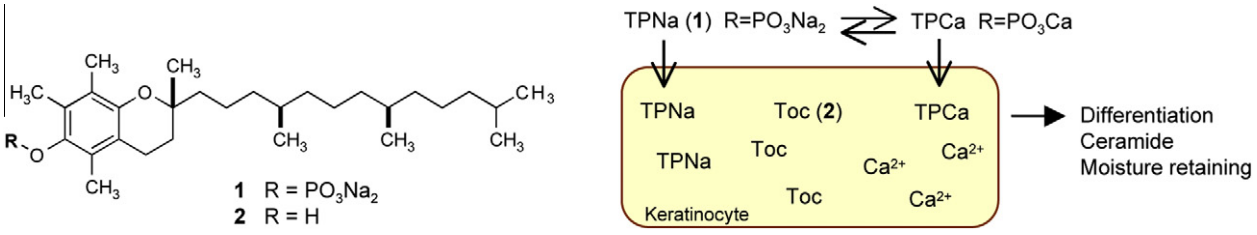
Inhibition of thioredoxin reductase by a novel series of bis-1,2-benzisoselenazol-3(2*H*)-ones: Organoselenium compounds for cancer therapy **pp 3816–3827**
Jie He, Dongdong Li, Kun Xiong, Yongjie Ge, Hongwei Jin, Guozhou Zhang, Mengshi Hong, Yongliang Tian, Jin Yin, Huihui Zeng*



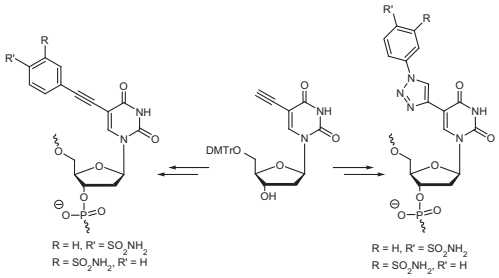
Chemical syntheses and in vitro antibacterial activity of two desferrioxamine B-ciprofloxacin conjugates with potential esterase and phosphatase triggered drug release linkers **pp 3828–3836**
Cheng Ji, Marvin J. Miller*



Improvement by sodium dl-α-tocopheryl-6-O-phosphate treatment of moisture-retaining ability in stratum corneum through increased ceramide levels **pp 3837–3842**
Eiko Kato, Noriko Takahashi*

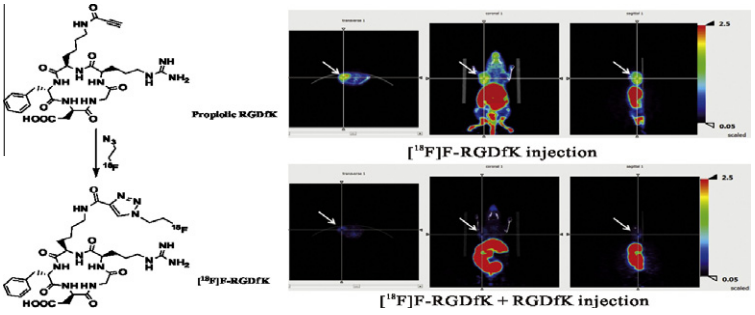


Sulfonamide bearing oligonucleotides: Simple synthesis and efficient RNA recognition **pp 3843–3849**
Pawan Kumar, Navneet Chandak, Poul Nielsen, Pawan K. Sharma*



Efficient π–π-stacking between two or more phenyltriazoles in the major groove was found to increase the thermal stability of a DNA:RNA duplex significantly. On the other hand, the alkynyl group was not as efficient in stacking as the triazolyl group.

Radiolabeling of RGD peptide and preliminary biological evaluation in mice bearing U87MG tumors **pp 3850–3855**
Jianbo Li, Lingli Shi, Lina Jia, Dawei Jiang, Wei Zhou, Weiqing Hu, Yujin Qi, Lan Zhang*



Design, synthesis, anti-HIV evaluation and molecular modeling of piperidine-linked amino-triazine derivatives as potent non-nucleoside reverse transcriptase inhibitors **pp 3856–3864**

Xuwang Chen, Peng Zhan, Xin Liu, Ziheng Cheng, Caicai Meng, Siyuan Shao, Christophe Pannecouque, Erik De Clercq, Xinyong Liu*

Piperidine-substituted amino-triazine derivatives were designed, introducing amino to the triazine ring and polar hydrophilic groups to the right wing, with excellent activity against wild-type HIV-1.

Design, synthesis and preliminary bioactivity studies of 1,3,4-thiadiazole hydroxamic acid derivatives as novel histone deacetylase inhibitors **pp 3865–3872**

Peng Guan, Feng'e Sun, Xuben Hou, Feng Wang, Fan Yi, Wenfang Xu, Hao Fang*

n=0, 2, 3, 4, 5, 6

Phenyl
Benzyl
Phenethyl
(E)-Styryl

6i IC_{50}=89nM (HDAC)

Targeting of polyplex to human hepatic cells by bio-nanocapsules, hepatitis B virus surface antigen L protein particles **pp 3873–3879**

Masaharu Somiya, Nobuo Yoshimoto, Masumi Iijima, Tomoaki Niimi, Takehisa Dewa, Joohee Jung, Shun'ichi Kuroda*

BNC-polyplex complexes could enter human hepatic cells specifically via the early infection mechanism of HBV, and exert endosomal escape through BNC-derived membrane fusion and the PEI-derived proton sponge effect.

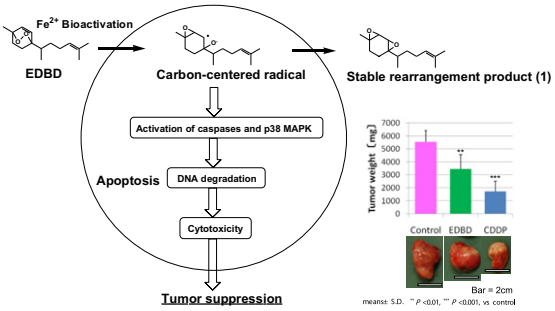
Synthesis and evaluation of 4- and 5-pyridazin-3-one phenoxypropylamine analogues as histamine-3 receptor antagonists **pp 3880–3886**

Nadine C. Becknell*, Jacquelyn A. Lyons, Lisa D. Aimone, Zeqi Huang, John A. Gruner, Rita Raddatz, Robert L. Hudkins

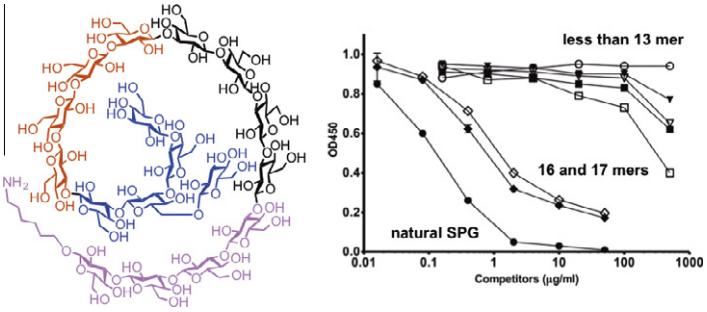
8a hH_3R K_i = 3 nM
rH_3R K_i = 9 nM

8b hH_3R K_i = 3 nM
rH_3R K_i = 4 nM

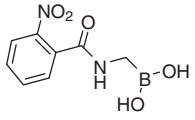
Cleavage mechanism and anti-tumor activity of 3,6-epidioxy-1,10-bisaboladiene isolated from edible wild plants **pp 3887–3897**
Ken-ichi Kimura*, Yoshimi Sakamoto, Nozomi Fujisawa, Shota Uesugi, Nobuhiro Aburai, Manabu Kawada, Shun-ichi Ohba, Takao Yamori, Eiko Tsuchiya, Hiroyuki Koshino



Synthesis of β(1,3) oligoglucans exhibiting a Dectin-1 binding affinity and their biological evaluation **pp 3898–3914**
Hiroshi Tanaka*, Tetsuya Kawai, Yoshiyuki Adachi, Shinya Hanashima, Yoshiki Yamaguchi, Naohito Ohno, Takashi Takahashi*

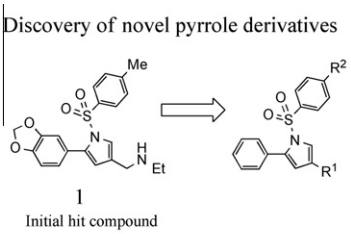


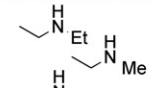
Synthesis and evaluation of boronic acids as inhibitors of Penicillin Binding Proteins of classes A, B and C **pp 3915–3924**
Astrid Zervosen*, André Bouillez, Alexandre Herman, Ana Amoroso, Bernard Joris, Eric Sauvage, Paulette Charlier, André Luxen



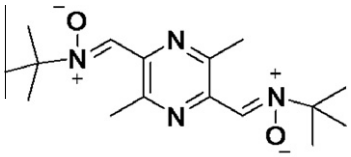
After the identification of (2,6-dimethoxybenzamido)methylboronic acid as a potent inhibitor of R39 from *Actinomadura* (IC_{50}: 1.3 μM) various acylaminomethylboronic acids were synthesized. (2-Nitrobenzamido)methylboronic acid inhibits Penicillin Binding Proteins of classes A, B and C.

Discovery, synthesis, and biological evaluation of novel pyrrole derivatives as highly selective potassium-competitive acid blockers **pp 3925–3938**
Haruyuki Nishida*, Atsushi Hasuoka, Yasuyoshi Arikawa, Osamu Kurasawa, Keizo Hirase, Nobuhiro Inatomi, Yasunobu Hori, Fumihiko Sato, Naoki Tarui, Akio Imanishi, Mitsuyo Kondo, Terufumi Takagi, Masahiro Kajino



R^1	R^2	H^+,K^+-ATPase inhibitory activities (IC_{50}, nM)
Compound 1		540
	Me	650
	Me	55
	OMe	30

Novel multi-functional nitrones for treatment of ischemic stroke **pp 3939–3945**
Yewei Sun, Gaoxiao Zhang, Zaijun Zhang, Pei Yu, Haijing Zhong, Jing Du, Yuqiang Wang*



Compound 21

OTHER CONTENTS

Bioorganic & Medicinal Chemistry Reviews and Perspectives **pp I–III**

*Corresponding author
Supplementary data available via SciVerse ScienceDirect

COVER

The membrane-bound 5-lipoxygenase-activating protein (FLAP) facilitates the transfer of arachidonic acid as substrate to 5-lipoxygenase (5-LO) leading to the biosynthesis of leukotrienes. Agents that interrupt this FLAP-mediated arachidonic acid transfer efficiently block leukotriene formation and have potential as anti-inflammatory and anti-allergic drugs. By using a rapid virtual screening approach based on a combined ligand- and structure-based FLAP pharmacophore, a benzimidazole derivative, bearing the isobutylphenylethyl fingerprint of ibuprofen as a new chemotype, was identified as potent suppressor of cellular leukotriene biosynthesis. [Banoglu, E.; Çalışkan; Luderer, S.; Gökçen, E.; Özkan, Y.; Altenhofen, W.; Weinigel, C.; Barz, D.; Gerstmeier, J.; Pergola, C.; Werz, O. *Bioorg. Med. Chem.,* **2012,** *20*, 3728–3741.]

Available online at www.sciencedirect.com

SciVerse ScienceDirect

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 SciVerse Scopus®. Full text available on SciVerse ScienceDirect®

ELSEVIER

ISSN 0968-0896