

Contents

Publisher's Announcement—Tetrahedron Prize for Creativity in Organic Chemistry for 2004

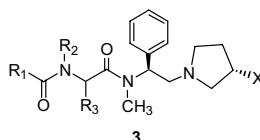
p 1277

COMMUNICATIONS

Amino acid conjugates as κ opioid receptor agonists

pp 1279–1282

Virendra Kumar,* Deqi Guo, Jeffrey D. Daubert, Joel A. Cassel, Robert N. DeHaven, Erik Mansson, Diane L. DeHaven-Hudkins and Alan L. Maycock

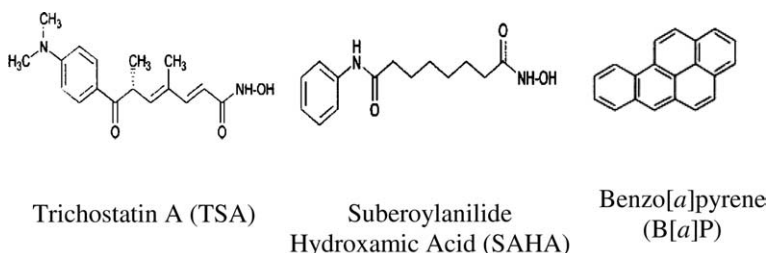


Amino acid conjugates of general structure **3** are described as kappa (κ) opioid receptor agonists. The leading κ agonists of the series have K_i values in the range of 0.83–6.7 nM.

Effects of suberoylanilide hydroxamic acid and trichostatin A on induction of cytochrome P450 enzymes and benzo[a]pyrene DNA adduct formation in human cells

pp 1283–1287

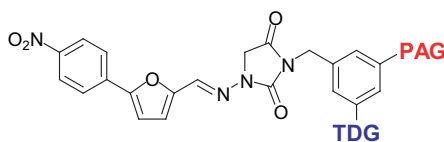
Louisa A. Hooven, Brinda Mahadevan, Channa Keshava, Christopher Johns, Cliff Pereira, Dhimant Desai, Shantu Amin, Ainsley Weston and William M. Baird*



Design of dantrolene-derived probes for radioisotope-free photoaffinity labeling of proteins involved in the physiological Ca^{2+} release from sarcoplasmic reticulum of skeletal muscle

pp 1289–1294

Takamitsu Hosoya, Toshiyuki Hiramatsu, Takaaki Ikemoto, Hiroshi Aoyama, Tatsuro Ohmae, Makoto Endo and Masaaki Suzuki*



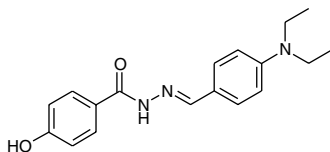
tag to introduce detectable group (TDG) = $-\text{CH}_2\text{N}_3$, $-\text{C}\equiv\text{CH}$
photo activatable group (PAG) = N_3 , $-\text{CCF}_3$
 $\text{N}=\text{N}$

Radioisotope-free photoaffinity probes selective for the physiological Ca^{2+} release from sarcoplasmic reticulum of skeletal muscle have been synthesized.

Identification of an agonist ligand for estrogen-related receptors ERR β/γ

pp 1311–1313

Donna D. Yu and Barry Marc Forman*

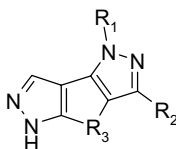


The synthesis of a selective ligand for the estrogen-related receptors ERR β/γ is reported.

**Benzodipyrroles: a new class of potent CDK2 inhibitors**

pp 1315–1319

Roberto D'Alessio,* Alberto Bargiotti, Suzanne Metz, M. Gabriella Brasca, Alexander Cameron, Antonella Ermoli, Aurelio Marsiglio, Paolo Polucci, Fulvia Roletto, Marcellino Tibolla, Michael L. Vazquez, Anna Vulpetti and Paolo Pevarello



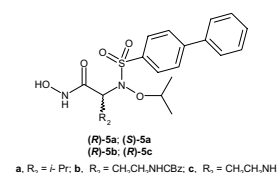
The synthesis and the preliminary structure–activity relationship results of this class are reported.

***N*-i-Propoxy-*N*-biphenylsulfonylaminobutylhydroxamic acids as potent and selective inhibitors of MMP-2 and MT1-MMP**

pp 1321–1326

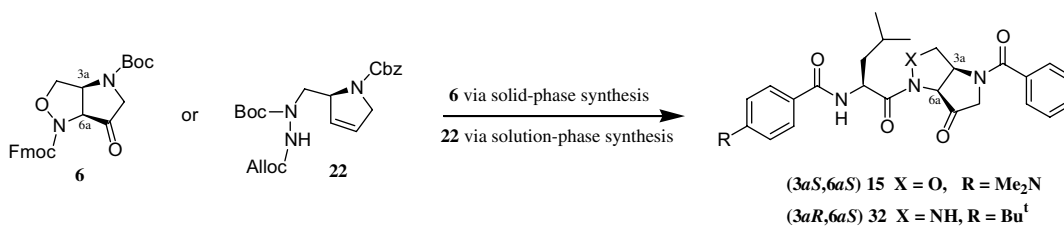
Armando Rossello,* Elisa Nuti, Paolo Carelli, Elisabetta Orlandini, Marco Macchia, Susanna Nencetti, Maurizio Zandomenighi, Federica Balzano, Gloria Uccello Barretta, Adriana Albini, Roberto Benelli, Giovanni Cercignani, Gillian Murphy and Aldo Balsamo

Structural manipulation of the pharmacophoric model of type A selective MMP inhibitors (MMPi), obtained by the insertion of some alkyl substituents R_2 possessing an appropriate geometry, steric bulkiness and lipophilicity, is able to improve potency, in the subnanomolar range on MMP-2, and to give a good MMP inhibition on MMP-14 (MT1-MMP) in the designed MMPi of type C, while maintaining a good MMP-1/MMP-2 selectivity profile. The simultaneous inhibition of these two enzymes yields type C compounds, which are potent antiangiogenic agents, able to block a chemoinvasion model on HUVEC cells under the micromolar range.

***cis*-6-Oxo-hexahydro-2-oxa-1,4-diazapentalene and *cis*-6-oxo-hexahydropyrrolo[3,2-*c*]pyrazole based scaffolds: design rationale, synthesis and cysteinyl proteinase inhibition**

pp 1327–1331

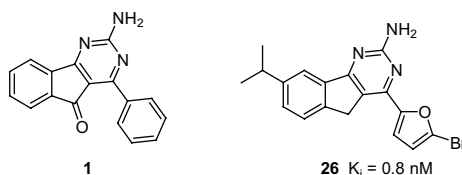
Yikang Wang, Alex Benn, Nick Flinn, Tracy Monk, Manoj Ramjee, John Watts and Martin Quibell*



The discovery and synthesis of novel adenosine receptor (A_{2A}) antagonists

pp 1333–1336

Julius J. Matasi, John P. Caldwell, Jinsong Hao, Bernard Neustadt, Leyla Arik, Carolyn J. Foster, Jean Lachowicz and Deen B. Tulshian*

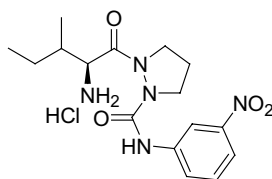


The structure–activity relationship investigation using **1** as a template led to the identification of a novel class of compounds as potent and selective antagonists of the A_{2A} receptor. Compound **26** was identified to be the most potent A_{2A} antagonist ($K_i = 0.8 \text{ nM}$) with 100-fold selectivity over the A_1 receptor.

Synthesis and evaluation of pyrazolidine derivatives as dipeptidyl peptidase IV (DP-IV) inhibitors

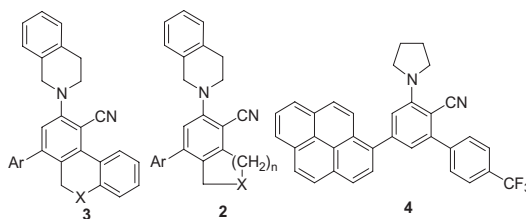
pp 1337–1340

Jin Hee Ahn,* Jin Ah Kim, Hye-Min Kim, Hyuk-Man Kwon, Sun-Chul Huh, Sang Dal Rhee, Kwang Rok Kim, Sung-Don Yang, Sung-Dae Park,* Jae Mok Lee, Sung Soo Kim and Hyae Gyeong Cheon

**Biaryls and heterobiaryls as α -glucosidase and protein tyrosine phosphatase inhibitors**

pp 1341–1344

Ashoke Sharon, Ramendra Pratap, Brajendra Tripathi, A. K. Srivastava, P. R. Maulik and Vishnu Ji Ram*

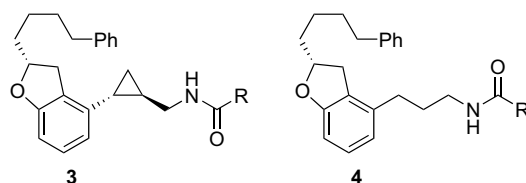


Synthesis and antihyperglycemic activity of biaryls are reported.

(*R*)-2-(4-Phenylbutyl)dihydrobenzofuran derivatives as melatoninerbic agents

pp 1345–1349

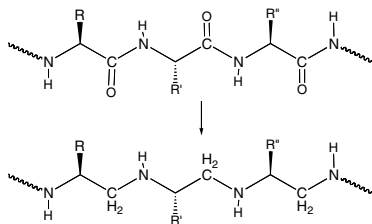
Li-Qiang Sun,* Katherine Takaki, Jie Chen, Stephen Bertenshaw, Lawrence Iben, Cathy D. Mahle, Elaine Ryan, Dedong Wu, Qi Gao and Cen Xu



(*R*)-2-(4-Phenylbutyl)dihydrobenzofuran derivatives (e.g., **3** and **4**) were synthesized as novel melatoninerbic ligands with significantly lower vasoconstrictive activity in vitro in the rat tail artery. Binding affinity assays were performed on cloned human MT_1 and MT_2 receptors stably expressed in NIH3T3 cells.

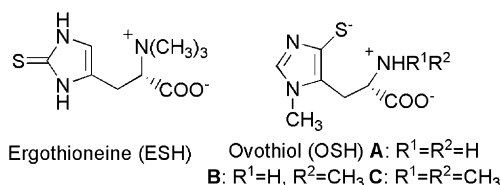
Chiral polyamines from reduction of polypeptides: asymmetric pyridoxamine-mediated transaminations pp 1351–1355

Wenjun Zhou, Nancy Yerkes, Jason J. Chroma, Lei Liu and Ronald Breslow*

**Ab initio studies of the properties of intracellular thiols ergothioneine and ovothiol**

pp 1357–1360

Christine E. Hand, Nicholas J. Taylor and John F. Honek*

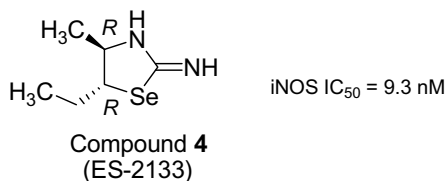


A detailed ab initio electronic structure analysis of ergothioneine and ovothiol is reported, which evaluates the thermodynamics of these thiols with alkyl thiols, hydroxide radicals, hydrogen peroxide and ascorbate.

**Novel and orally bioavailable inducible nitric oxide synthase inhibitors: synthesis and evaluation of optically active 4,5-dialkyl-2-iminoselenazolidine derivatives**

pp 1361–1366

Shigeo Ueda,* Hideo Terauchi, Kenji Suzuki, Akihiro Yano, Masashi Matsumoto, Taeko Kubo, Hisao Minato, Yukiyo Arai, Jun-ichi Tsuji and Nobuhide Watanabe



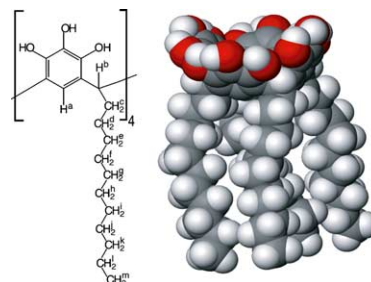
The synthesis and evaluation of compound **4** (ES-2133) and its related optically active compounds as iNOS inhibitor is reported. In addition, an alternative synthetic method to the selected compound **4** and its pharmacokinetic profile is also reported.

**Interaction of dopamine and acetylcholine with an amphiphilic resorcinarene receptor in aqueous micelle system**

pp 1367–1370

Makoto Demura,* Tsutomu Yoshida, Takatsugu Hirokawa, Yasuhiro Kumaki, Tomoyasu Aizawa, Katsutoshi Nitta, Isván Bitter and Klára Tóth

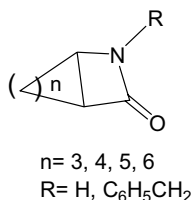
Molecular recognition of neurotransmitters with an amphiphilic resorcinarene receptor in an aqueous micelle system is studied by ¹H NMR measurements and theoretical chemical shift calculation.



Design, synthesis and biological evaluation of novel bicyclic β -lactams as potential antimalarials

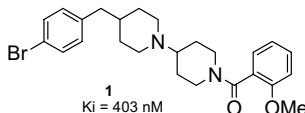
pp 1371–1373

Manisha Nivsarkar, D. Thavaselvam, S. Prasanna, Mamta Sharma and M. P. Kaushik*

**The synthesis of substituted biperidine amide compounds as CCR3 antagonists**

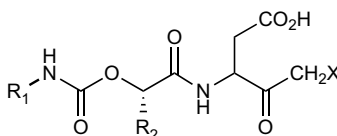
pp 1375–1378

Pauline C. Ting,* Joe F. Lee, Jie Wu, Shelby P. Umland, Robert Aslanian, Jianhua Cao, Youhao Dong, Charles G. Garlisi, Eric J. Gilbert, Ying Huang, James Jakway, Joseph Kelly, Zhidan Liu, Stuart McCombie, Himanshu Shah, Fang Tian, Yuntao Wan and Neng-Yang Shih

The structure–activity relationship of biperidine **1** as a CCR3 antagonist has been evaluated.**Dipeptidyl aspartyl fluoromethylketones as potent caspase inhibitors: peptidomimetic replacement of the P_2 α -amino acid by a α -hydroxy acid**

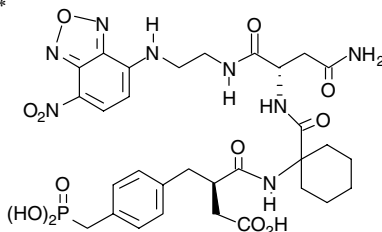
pp 1379–1383

Yan Wang, Lufeng Guan, Shaojuan Jia, Ben Tseng, John Drewe and Sui Xiong Cai*

The synthesis and biological evaluation of a group of peptidomimetic α -carbamoyl-alkylcarbonyl-aspartyl fluoromethylketones as caspase inhibitors is reported.**Utilization of a nitrobenzoxadiazole (NBD) fluorophore in the design of a Grb2 SH2 domain-binding peptide mimetic**

pp 1385–1388

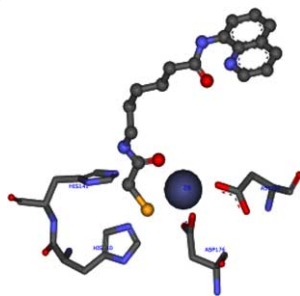
Zhen-Dan Shi, Rajeshri G. Karki, Shinya Oishi, Karen M. Worthy, Lakshman K. Bindu, Pathirage G. Dharmawardana, Marc C. Nicklaus, Donald P. Bottaro, Robert J. Fisher and Terrence R. Burke, Jr.*

Grb2 SH2 Domain $K_D = 119 \pm 0.6 \text{ nM}$

Chemistry and biology of mercaptoacetamides as novel histone deacetylase inhibitors

pp 1389–1392

Bin Chen, Pavel A. Petukhov, Mira Jung, Alfredo Velena, Elena Eliseeva, Anatoly Dritschilo and Alan P. Kozikowski*

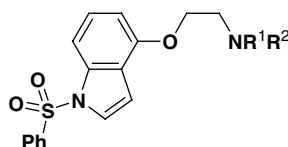


Mercaptoacetamides were designed and synthesized as HDAC inhibitors.

4-(2-Aminoethoxy)-*N*-(phenylsulfonyl)indoles as novel 5-HT₆ receptor ligands

pp 1393–1396

Ping Zhou,* Yinfu Yan, Ronald Bernotas, Boyd L. Harrison, Donna Huryn, Albert J. Robichaud, Guo Ming Zhang, Deborah L. Smith and Lee E. Schechter



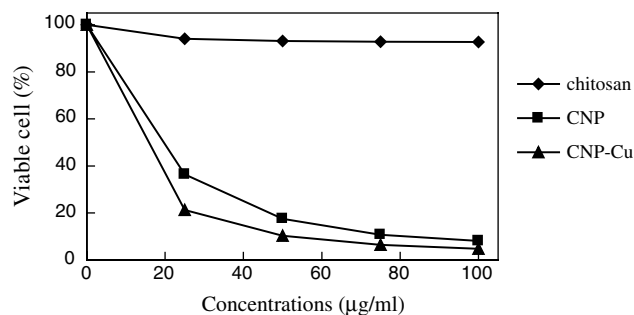
The preparation of a novel class of 4-(2-aminoethoxy)-*N*-(phenylsulfonyl)indoles which exhibit high affinity towards the 5-HT₆ receptor is reported.

Cytotoxic activities of chitosan nanoparticles and copper-loaded nanoparticles

pp 1397–1399

Lifeng Qi,* Zirong Xu, Xia Jiang, Yan Li and Minqi Wang

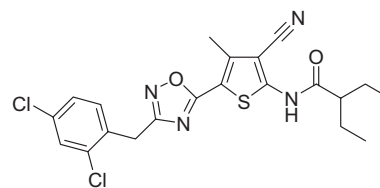
Cytotoxic activities of the chitosan, chitosan nanoparticles (mean particle size = 40 nm) and copper-loaded chitosan nanoparticles with various concentrations against BEL7402 cell line. CNP = chitosan nanoparticles; CNP-Cu = copper-loaded chitosan nanoparticles. Each value represents the mean of triplicate measurements and varied from the mean by not more than 10%.

**Discovery and investigation of a novel class of thiophene-derived antagonists of the human glucagon receptor**

pp 1401–1405

Joseph L. Duffy,* Brian A. Kirk, Zenon Konteatis, Elizabeth L. Campbell, Rui Liang, Edward J. Brady, Mari Rios Candellere, Victor D. H. Ding, Guoqiang Jiang, Frank Liu, Sajjad A. Qureshi, Richard Saperstein, Deborah Szalkowski, Sharon Tong, Lauri M. Tota, Dan Xie, Xiaodong Yang, Peter Zafian, Song Zheng, Kevin T. Chapman, Bei B. Zhang and James R. Tata

A novel class of antagonists of the human glucagon receptor (hGCGR) has been discovered. An SAR exploration of the lead class resulted in **13**, which exhibited good potency as an hGCGR functional antagonist (IC₅₀ = 34 nM) and moderate bioavailability (36% in mice).

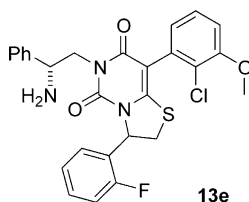


13 cAMP IC₅₀ = 34 nM

Efficient synthesis of bicyclic oxazolino- and thiazolino[3,2-c]pyrimidine-5,7-diones and its application to the synthesis of GnRH antagonists

pp 1407–1411

Joseph Pontillo* and Chen Chen



Treatment of various 2-methyl oxazolines or thiazolines with chlorocarbonyl isocyanate gives the corresponding bicyclic oxazolino- or thiazolino[3,2-c]pyrimidin-5,7-dione derivatives in very good yield. This reaction has been applied to the rapid syntheses of human gonadotropin-releasing hormone (*h*GnRH) receptor antagonists for SAR study, resulting in **13e** with binding affinity in the low nanomolar range (4.5 nM).

Protein microarray using α -amino acids as metal tags on chips

pp 1413–1416

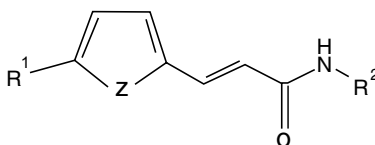
Supachok Sinchaikul, Fu-Ming Pan, Ching-Wen Cheng, Chi-Huey Wong, Jim-Min Fang, Min-Jen Tseng and Shui-Tein Chen*

Procedures for synthesizing α -amino acids on a chip for coordination with transitional metal ions and a His-Tagged protein have been successfully developed as a stable protein microarray. Using the recombinant His-Tagged 3CL-protease (3CL^{Pro}) as a model for attachment to chips containing D-/L-Glu, Asp, Orn, Ser via different transitional metal ions, it was found that the Orn chip was the best of affinity binding and stability by which Zn²⁺ was the best metal ion for affinity while Co²⁺ was the best metal ion for stability. Thus, this protein microarray can be alternatively used as a high throughput screening method for rapid detection against SARS CoV 3CL^{Pro} and/or efficient purification of other Tagged proteins.

Synthesis and in vitro antitrypanosomal activity of novel Nifurtimox analogues

pp 1417–1421

Rocío Pozas, Javier Carballo, Clementina Castro and Julieta Rubio*

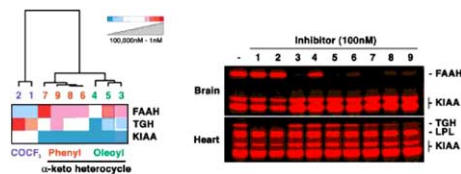


Eight novel Nifurtimox analogues were synthesized and tested in vitro against *Trypanosoma cruzi* epimastigotes.

Discovery of an exceptionally potent and selective class of fatty acid amide hydrolase inhibitors enlisting proteome-wide selectivity screening: concurrent optimization of enzyme inhibitor potency and selectivity

pp 1423–1428

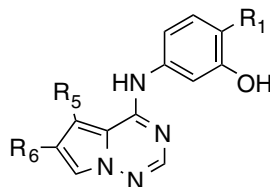
Donmienne Leung, Wu Du, Christophe Hardouin, Heng Cheng, Inkyu Hwang, Benjamin F. Cravatt and Dale L. Boger*



Synthesis and SAR of 4-(3-hydroxyphenylamino)pyrrolo[2,1-f][1,2,4]triazine based VEGFR-2 kinase inhibitors

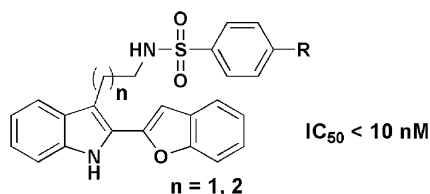
pp 1429–1433

Robert M. Borzilleri, Zhen-wei Cai, Christopher Ellis, Joseph Fargnoli, Abera Fura, Tracy Gerhardt, Bindu Goyal, John T. Hunt, Steven Mortillo, Ligang Qian, John Tokarski, Viral Vyas, Barri Wautlet, Xioping Zheng and Rajeev S. Bhide*

**Tryptamine and homotryptamine-based sulfonamides as potent and selective inhibitors of 15-lipoxygenase**

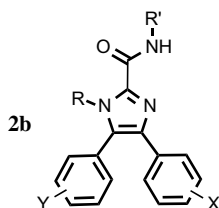
pp 1435–1440

David S. Weinstein,* Wen Liu, Zhengxiang Gu, Charles Langevine, Khehyong Ngu, Leena Fadnis, Donald W. Combs, Doree Sitkoff, Saleem Ahmad, Shaobin Zhuang, Xing Chen, Feng-Lai Wang, Deborah A. Loughney, Karnail S. Atwal, Robert Zahler, John E. Macor, Cort S. Madsen and Natesan Murugesan*

**Synthesis and activity of 4,5-diarylimidazoles as human CB1 receptor inverse agonists**

pp 1441–1446

Christopher W. Plummer,* Paul E. Finke, Sander G. Mills, Junying Wang, Xinchun Tong, George A. Doss, Tung M. Fong, Julie Z. Lao, Marie-Therese Schaeffer, Jing Chen, Chun-Pyn Shen, D. Sloan Stribling, Lauren P. Shearman, Alison M. Strack and Lex H. T. Van der Ploeg

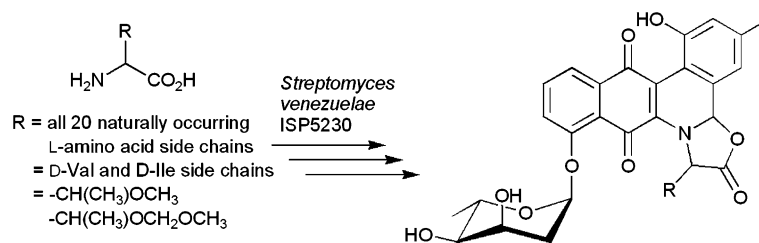


The synthesis and structure–activity relationships for a series of substituted 4,5-diphenylimidazole-2-carboxamide derivatives **2b** as selective, orally active human CB1 inverse agonists are described.

**Novel jadomycins: incorporation of non-natural and natural amino acids**

pp 1447–1449

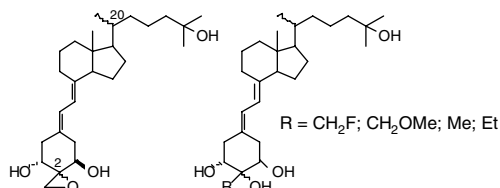
David L. Jakeman,* Spring Farrell, Wendy Young, René J. Doucet and Shannon C. Timmons



New derivatives of 1 α ,25-dihydroxy-19-norvitamin D₃ with two substituents at C-2: synthesis and biological activity

pp 1451–1455

Masato Shimizu,* Yukiko Iwasaki, Mika Shimazaki, Youhei Amano, Keiko Yamamoto, Wolfgang Reischl and Sachiko Yamada

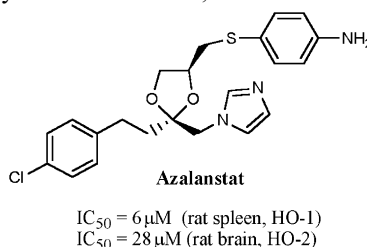


Novel 2,2-disubstituted 19-norvitamin D₃ analogs were synthesized and their binding affinity to the vitamin D receptor and transcriptional activity were evaluated.

Synthesis and evaluation of azalanstat analogues as heme oxygenase inhibitors

pp 1457–1461

Jason Z. Vlahakis, Robert T. Kinobe, Raymond J. Bowers, James F. Brien, Kanji Nakatsu and Walter A. Szarek*

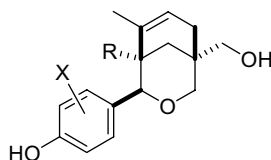


The synthesis and biological activity of novel heme oxygenase (HO) inhibitors based on the lead structure of azalanstat is presented. Potency and selectivity in the inhibition of HO-1 and HO-2 isozymes were found to be dependent on the configurational and structural features of these compounds.

Structure–activity relationships and sub-type selectivity in an oxabicyclic estrogen receptor α/β agonist scaffold

pp 1463–1466

Lawrence G. Hamann,* J. Hoyt Meyer, Daniel A. Rupp, Keith B. Marschke, Francisco J. Lopez, Elizabeth A. Allegretto and Donald S. Karanewsky*

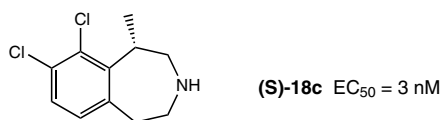


The synthesis and estrogen receptor α/β agonist activity of compounds from this novel scaffold are reported.

Discovery and SAR of new benzazepines as potent and selective 5-HT_{2C} receptor agonists for the treatment of obesity

pp 1467–1470

Brian M. Smith,* Jeffrey M. Smith, James H. Tsai, Jeffrey A. Schultz, Charles A. Gilson, Scott A. Estrada, Rita R. Chen, Douglas M. Park, Emily B. Prieto, Charlemagne S. Gallardo, Dipanjan Sengupta, William J. Thomsen, Hazel R. Saldana, Kevin T. Whelan, Frederique Menzaghi, Robert R. Webb and Nigel R. A. Beeley

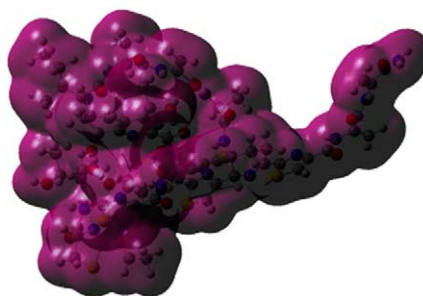


The synthesis and SAR of a 3-benzazepine series of selective 5-HT_{2C} agonists is described.

Electronic structure calculations on the thiazole-containing antibiotic thiostrepton: molecular mechanics, semi-empirical and ab initio analyses

pp 1471–1474

Pei C. Hang and John F. Honek*

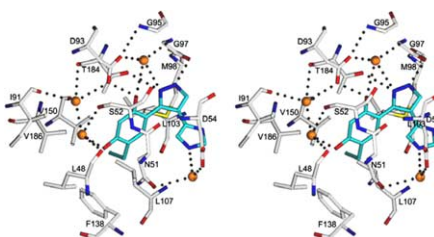


Data from computational analyses utilizing molecular mechanics, molecular dynamics, semi-empirical and ab initio methods on the peptide antibiotic thiostrepton are reported.

**Crystal structures of human HSP90 α -complexed with dihydroxyphenylpyrazoles**

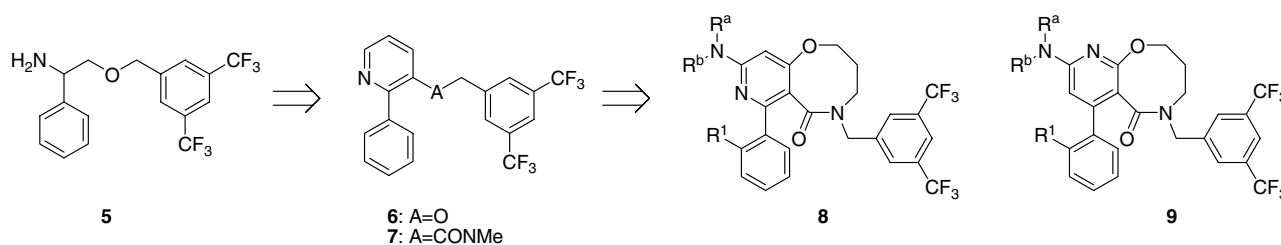
pp 1475–1478

Andreas Kreusch, Shulin Han, Achim Brinker, Vicki Zhou, Ha-soon Choi, Yun He, Scott A. Lesley, Jeremy Caldwell and Xiang-ju Gu*

**Design and synthesis of novel 9-substituted-7-aryl-3,4,5,6-tetrahydro-2H-pyrido[4,3-*b*]- and [2,3-*b*]-1,5-oxazocin-6-ones as NK₁ antagonists**

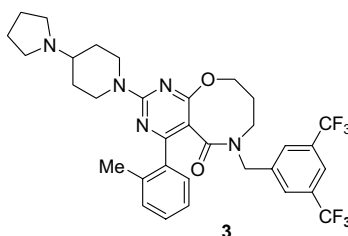
pp 1479–1484

Shigeki Seto,* Asao Tanioka, Makoto Ikeda and Shigeru Izawa

**2-Substituted-4-aryl-6,7,8,9-tetrahydro-5H-pyrimido[4,5-*b*][1,5]oxazocin-5-one as a structurally new NK₁ antagonist**

pp 1485–1488

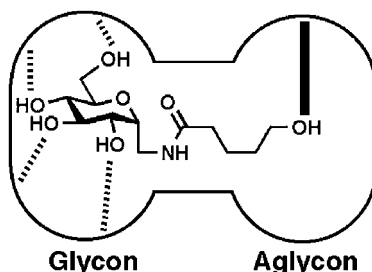
Shigeki Seto,* Asao Tanioka, Makoto Ikeda and Shigeru Izawa



Aglycon specificity profiling of α -glucosidases using synthetic probes

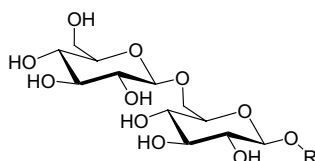
pp 1489–1492

Wataru Hakamata,* Makoto Muroi, Kazunari Kadokura, Toshiyuki Nishio, Tadatake Oku, Atsuo Kimura, Seiya Chiba and Akira Takatsuki

**Synthesis and evaluation of diverse analogs of amygdalin as potential peptidomimetics of peptide T**

pp 1493–1496

Eyleen Araya, Alex Rodriguez, Jaime Rubio, Alessandro Spada, Jesus Joglar, Amadeu Llebaria, Carmen Lagunas, Andres G. Fernandez, Susanna Spisani and Juan J. Perez*

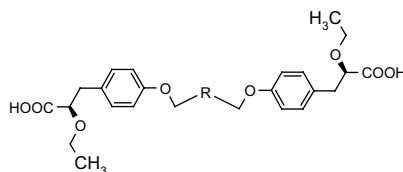


The synthesis of amygdalin analogs as peptidomimetics of peptide T is reported.

**Structure–activity relationships of dimeric PPAR agonists**

pp 1497–1500

Per Sauerberg,* John P. Mogensen, Lone Jeppesen, L. Anders Svensson, Jan Fleckner, Jan Nehlin, Erik M. Wulff and Ingrid Pettersson

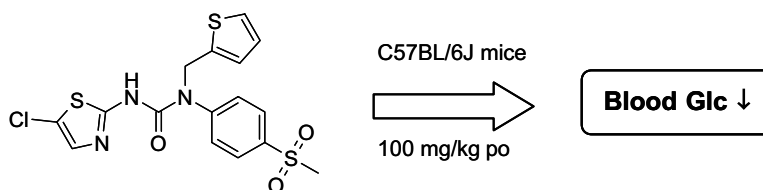


The SAR of dimeric PPAR agonists is reported.

Glucokinase-activating ureas

pp 1501–1504

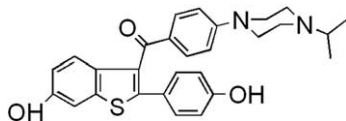
Arlindo L. Castelhana, Hanqing Dong, Matthew C. T. Fyfe,* Lisa S. Gardner, Yukari Kamikozawa, Satomi Kurabayashi, Masao Nawano, Rikiya Ohashi, Martin J. Procter, Li Qiu, Chrystelle M. Rasamison, Karen L. Schofield, Vilas K. Shah, Kiichiro Ueta, Geoffrey M. Williams, David Witter and Kosuke Yasuda



Ureas that lower blood glucose levels in vivo by activating glucokinase are described.

Benzothiophenes containing a piperazine side chain as selective ligands for the estrogen receptor α and their bioactivities in vivo pp 1505–1507

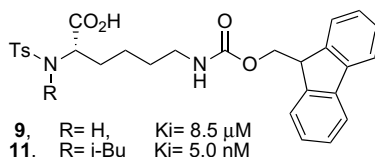
Chunhao Yang,* Guangyu Xu, Jia Li, Xihan Wu, Bo Liu, Xueming Yan, Mingwei Wang* and Yuyuan Xie



Benzothiophenes bearing piperazine side chains were synthesized and identified to be high-affinity ligands with high selectivity for ER α subtype, and they were potent agonists in bone tissue.

Lysine derivatives as potent HIV protease inhibitors. Discovery, synthesis and structure–activity relationship studies pp 1509–1513

Abderrahim Bouzide,* Gilles Sauvé and Jocelyn Yelle



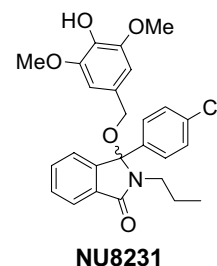
A screening assay program carried out on commercially available N-protected amino acids showed that *N* α -sulfonamide-*N* ϵ -Fmoc-L-lysine **9** displayed an 8.5 μ M inhibition constant. Addition of an isobutyl group at the *N* α -position allowed the discovery of the lead candidate **11** exhibiting a 5.0 nM K_i . The discovery, synthesis and SAR studies are described.

Isoindolinone-based inhibitors of the MDM2–p53 protein–protein interaction

pp 1515–1520

Ian R. Hardcastle,* Shafiq U. Ahmed, Helen Atkins, A. Hilary Calvert, Nicola J. Curtin, Gillian Farnie, Bernard T. Golding, Roger J. Griffin, Sabrina Guyenne, Claire Hutton, Per Källblad, Stuart J. Kemp, Martin S. Kitching, David R. Newell, Stefano Norbedo, Julian S. Northen, Rebecca J. Reid, K. Saravanan, Henriëtte M. G. Willems and John Lunec*

The design, synthesis and evaluation of 24 isoindolinones as potential inhibitors of the MDM2–p53 interaction is described. The most potent inhibitor NU8231 (ELISA: $IC_{50} = 5.3 \pm 0.9 \mu$ M) displays cellular activity in human SJSA cells.

**In vivo incorporation of an alkyne into proteins in *Escherichia coli***

pp 1521–1524

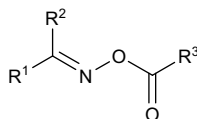
Alexander Deiters and Peter G. Schultz*



A bioconjugation using a genetically encoded alkyne in *Escherichia coli* is reported.

(E)-Phenyl- and -heteroaryl-substituted O-benzoyl- (or acyl)oximes as lipoprotein-associated phospholipase A₂ inhibitors**pp 1525–1527**

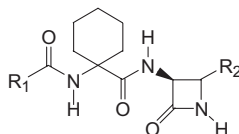
Tae-Sook Jeong, Mi Jeong Kim, Hana Yu, Kyung Soon Kim, Joong-Kwon Choi, Sung-Soo Kim and Woo Song Lee*

R¹ = Ar, Het; R² = H, Me, Ph; R³ = Ar, alkyl

A series of (*E*)-phenyl- and -heteroaryl-substituted *O*-benzoyl- (or acyl)oximes **3a–n** were synthesized and evaluated for their inhibitory activities on Lp-PLA₂.

3,4-Disubstituted azetidinones as selective inhibitors of the cysteine protease cathepsin K. Exploring P3 elements for potency and selectivity**pp 1529–1534**

Eduardo L. Setti,* Dana Davis, James W. Janc, Douglas A. Jeffery, Harry Cheung and Walter Yu



The synthesis of a series of highly potent and selective inhibitors of cathepsin K based on the azetidin-2-one warhead is reported.

OTHER CONTENTS**Contributors to this issue**
Instructions to contributors**pp I–II**
pp III–VI

*Corresponding author

i+ Supplementary data available via ScienceDirect

COVER

Proteome screening for FAAH selectivity. (Left) Comparison of the potencies and relative selectivities of FAAH inhibitors. IC₅₀ values are clustered into three classes: highly potent and highly selective α -ketoheterocycle inhibitors with phenyl side chain (red), moderately potent α -ketoheterocycle inhibitors with oleoyl side chain (green) and trifluoromethyl ketone inhibitors selective for TGH (purple). (Right) Competitive profiling of FAAH inhibitors (100 nM) with RFP (100 nM) in brain and heart membrane proteome [Leung, D.; Du, W.; Hardouin, C.; Cheng, H.; Hwang, I.; Cravatt, B. J.; Boger, D. L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1423].

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ISSN 0960-894X