

Contents

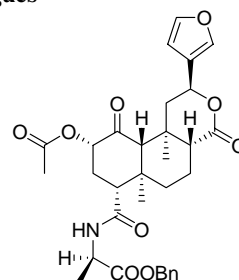
ARTICLES

Synthesis and in vitro pharmacological studies of C(4) modified salvinorin A analogues

pp 4169–4173

David Y. W. Lee, Minsheng He, Leelakrishna Kondaveti, Lee-Yuan Liu-Chen, Zhongze Ma, Yulin Wang, Yong Chen, Jian-Guo Li, Cecile Beguin, William A. Carlezon, Jr. and Bruce Cohen*

A series of salvinorin A derivatives modified at the C(4) position were prepared and screened for binding and functional activities at the human κ -opioid receptor. Several highly selective κ -full agonists are reported.



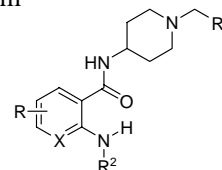
18a $K_i = 26.9$ nM
 $ED_{50} = 46.7$ nM

Identification of *ortho*-amino benzamides and nicotinamides as MCHR1 antagonists

pp 4174–4179

Anil Vasudevan,* Matthew J. LaMarche,* Christopher Blackburn, Jennifer Lee Che, Courtney A. Luchaco-Cullis, Sujen Lai, Thomas H. Marsilje, Michael A. Patane, Andrew J. Souers, Derek Wodka, Bradley Geddes, Sumiao Chen, Seven Brodjian, Doug H. Falls, Brian D. Dayton, Eugene Bush, Michael Brune, Robin D. Shapiro, Kennan C. Marsh, Lisa E. Hernandez, Hing L. Sham, Christine A. Collins and Philip R. Kym

Several potent and efficacious MCHR1 antagonists containing an *ortho*-amino benzamide or nicotinamide chemotype have been identified, exemplified by **28** and **50**.

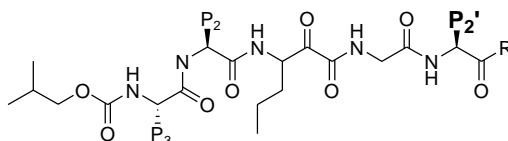


Hepatitis C virus NS3-4A serine protease inhibitors: SAR of P₂' moiety with improved potency

pp 4180–4184

A. Arasappan,* F. G. Njoroge, T.-Y. Chan,* F. Bennett, S. L. Bogen, K. Chen, H. Gu, L. Hong, E. Jao, Y.-T. Liu, R. G. Lovey, T. Parekh, R. E. Pike, P. Pinto, B. Santhanam, S. Venkatraman, H. Vaccaro, H. Wang, X. Yang, Z. Zhu, B. Mckittrick, A. K. Saksena, V. Girijavallabhan, J. Pichardo, N. Butkiewicz, R. Ingram, B. Malcolm, A. Prongay, N. Yao, B. Marten, V. Madison, S. Kemp, O. Levy, M. Lim-Wilby, S. Tamura and A. K. Ganguly

Introduction of appropriate amino acid derivatives at P₂' position improved the binding potency of P₃-capped α -ketoamide inhibitors of HCV NS3 serine protease. X-ray crystal structure of one of the inhibitors (**43**) bound to the protease revealed the importance of the P₂' moiety.

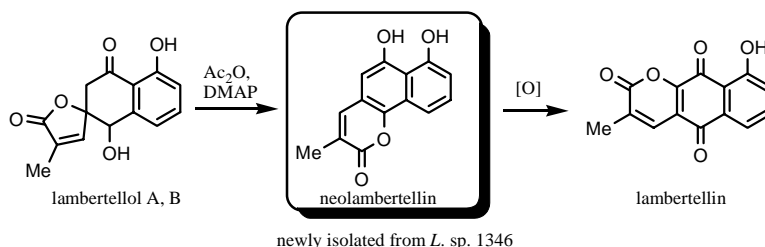


P₃ = Val or Chg
P₂ = Pro or Leu
P₂' = varied
R' = NH₂ or OH

Isolation, structure elucidation, preparation, and biological properties of neolambertellin

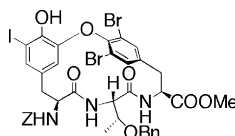
pp 4185–4188

Takanori Murakami, Masaru Hashimoto* and Toshikatsu Okuno

**Discovery of halogenated euryamide B analogues as inhibitors of lipid droplet accumulation in macrophages**

pp 4189–4191

Rika Obata, Taichi Ohshiro, Hiroshi Tomoda and Shigeru Nishiyama*

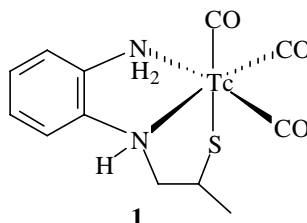


The synthetic euryamide B analogues possessed effective inhibitory activity against the lipid droplet accumulation in macrophages.

Characterisation and biodistribution of two neutral $^{99\text{m}}\text{Tc}(\text{CO})_3$ complexes with a tridentate ligand

pp 4192–4195

Dirk Rattat, Bernard Cleynhens, Guy Bormans, Christelle Terwinghe and Alfons Verbruggen*



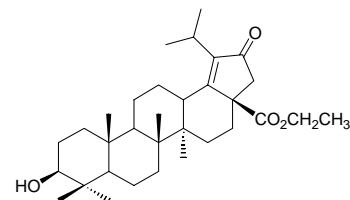
N-(2-Mercapto-propyl)-1,2-phenylenediamine (MPPDA) and *N*- β -aminoethylglycine (AEG) were labelled with $^{99\text{m}}\text{Tc}(\text{CO})_3^+$ to form the neutral complexes $[\text{MPPDA}]$ (1) and $[\text{AEG}]$, which were analysed by LC–MS. Their biodistribution in mice was studied.

Correlation of cytotoxic activity of betulinines and their hydroxy analogues

pp 4196–4200

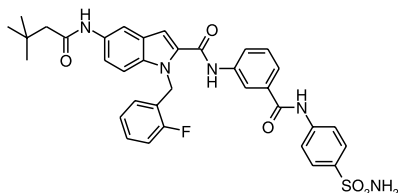
Jan Sarek,* Miroslav Kvasnica, Milan Urban, Jiri Klinot and Marian Hajduch

This research is based on intention to prepare and test 3β -hydroxy and $3\beta,28$ -dihydroxy analogs of new pro-apoptotic derivatives (betulinines) using selective hydrolysis procedure and strategic-protective groups. The evaluation of cytotoxicity of prepared compounds on several tumor cell lines using an MTT test was our interest. It was found that hydrolysis of acetates in betulinines afforded compounds with higher cytotoxicity in case of 18-lupene-21-ones (e.g., ethyl 3β -hydroxy-21-oxolup-18-en-28-oate), whereas hydrolysis of the 18-lupene-21,22-diones gave less active derivatives.



Novel, selective indole-based ECE inhibitors: Lead optimization via solid-phase and classical synthesis pp 4201–4205

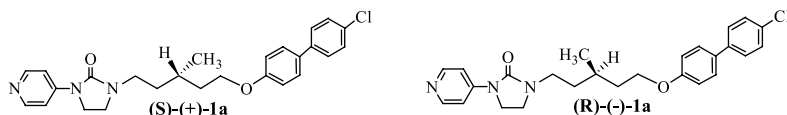
Michael Brands,* Jens-Kerim Ergüden, Kentaro Hashimoto, Dirk Heimbach,
Christian Schröder, Stephan Siegel, Johannes-Peter Stasch and Stefan Weigand



A novel class of indole-based endothelin-converting enzyme (ECE) inhibitors was identified by high throughput screening. We report systematic optimization of this compound class by means of classical and solid-phase chemistry. Optimized compounds with a bisarylamide side chain at the 2-position of the indole skeleton exhibit low-nanomolar activity on ECE.

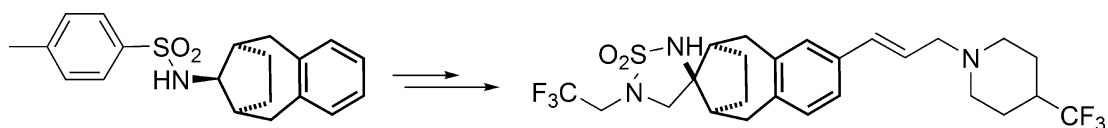
Synthesis and antipicornavirus activity of (*R*)- and (*S*)-1-[5-(4'-chlorobiphenyl-4-yloxy)-3-methylpentyl]-3-pyridin-4-yl-imidazolidin-2-one pp 4206–4211

Jyh-Haur Chern,* Chih-Shiang Chang, Chia-Liang Tai, Yen-Chun Lee,
Chung-Chi Lee, Iou-Jiun Kang, Ching-Yin Lee and Shin-Ru Shih*

**Cyclic sulfamide γ -secretase inhibitors**

pp 4212–4216

Tim Sparey,* Dirk Beher, Jonathan Best, Mirlinda Biba, José L. Castro, Earl Clarke,
Joanne Hannam, Timothy Harrison, Huw Lewis, Andrew Madin, Mark Shearman,
Bindi Sohal, Nancy Tsou, Christopher Welch and Jonathan Wrigley



A novel series of *N*-alkyl-substituted cyclic sulfamides were developed from a screening hit.

Design, synthesis and structure–activity relationship of a series of fragment analogues of antistasin (ATS) and ghilantens (GLS) pp 4217–4220

Dancho L. Danalev,* Lybomir T. Vezekov and Boryana Grigorova

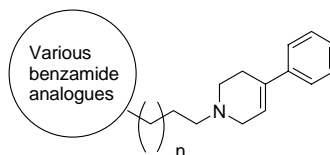
The designed and synthesized anticoagulant activity and structure–activity relationship of a series of low molecular weight peptide inhibitors of Factor Xa, fragment analogues of ATS and GLS, is reported. The newly synthesized peptides have the following structure:

H-X-Pro-Lys-Arg-Lys-Leu-Val-Pro-Y (X=Arg, Lys, Orn or missed and Y=OH, NH₂).

4-Phenyl-1,2,3,6-tetrahydropyridine, an excellent fragment to improve the potency of PARP-1 inhibitors

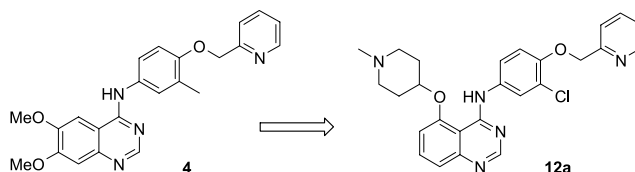
pp 4221–4225

Junya Ishida,* Kouji Hattori, Hirofumi Yamamoto, Akinori Iwashita, Kayoko Mihara and Nobuya Matsuoka


5-Substituted 4-anilinoquinazolines as potent, selective and orally active inhibitors of erbB2 receptor tyrosine kinase

pp 4226–4229

Peter Ballard, Robert H. Bradbury,* Laurent F. A. Hennequin, D. Mark Hickinson, Paul D. Johnson, Jason G. Kettle, Teresa Klinowska, Remy Morgentin, Donald J. Ogilvie and Annie Olivier

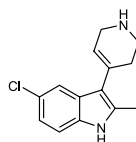


Starting from a 6,7-substituted quinazoline lead **4**, optimisation of 5-substituted quinazolines containing an extended aniline motif led to potent and selective inhibitors of erbB2 receptor tyrosine kinase, and a representative compound **12a** inhibited tumour growth in a mouse xenograft model.

2-Alkyl-3-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indoles as novel 5-HT₆ receptor agonists

pp 4230–4234

Cecilia Mattsson,* Clas Sonesson, Anna Sandahl, Hartmut E. Greiner, Michael Gassen, Jörg Plaschke, Joachim Leibrock and Henning Böttcher

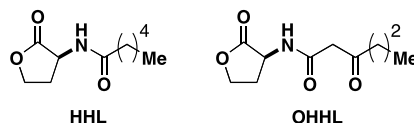


A series of 2-alkyl-3-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indoles was synthesized and evaluated for their 5-HT₆ activity. The most potent agonist in this series was 5-chloro-2-methyl-3-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indole with an IC₅₀ = 7.4 nM in ³H-LSD-binding and an EC₅₀ = 1.0 nM in a functional assay measuring production of cyclic AMP.

Structure–activity relationships of *Erwinia carotovora* quorum sensing signaling molecules

pp 4235–4238

Martin Welch, Jenny M. Dutton, Freija G. Glansdorp, Gemma L. Thomas, Debra S. Smith, Sarah J. Coulthurst, Anne M. L. Barnard, George P. C. Salmond and David R. Spring*



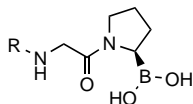
Quorum sensing modulators were synthesized and screened in vivo in the phytopathogen *Erwinia carotovora*. The biological activity of each compound was correlated with its ability to bind *Erwinia* quorum sensing receptor proteins (LuxR homologues) in vitro.



Synthesis and structure–activity relationship of *N*-alkyl Gly-boro-Pro inhibitors of DPP4, FAP, and DPP7

pp 4239–4242

Yi Hu, Lifu Ma, Min Wu, Melissa S. Wong, Bei Li, Sergio Corral, Zhizhou Yu, Tyzoon Nomanbhoy, Senaiet Alemayehu, Stacy R. Fuller, Jonathan S. Rosenblum, Natasha Rozenkrants, Lauro C. Minimo, William C. Ripka, Anna K. Szardenings, John W. Kozarich and Kevin R. Shreder*

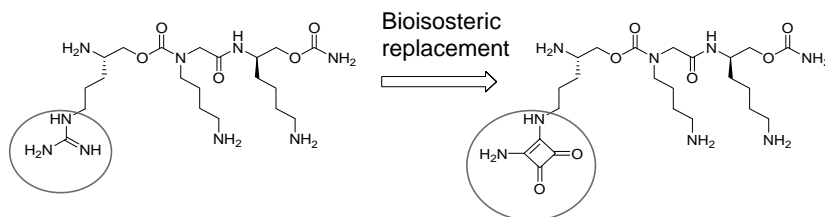


The structure-activity relationship of various *N*-alkyl Gly-boro-Pro derivatives against three dipeptidyl peptidases (DPP4, FAP, and DPP7) was explored.

Design and synthesis of a novel peptidomimetic inhibitor of HIV-1 Tat–TAR interactions: Squaryldiamide as a new potential bioisostere of unsubstituted guanidine

pp 4243–4246

Chi-Wan Lee, Hong Cao, Kozi Ichiyama and Tariq M. Rana*

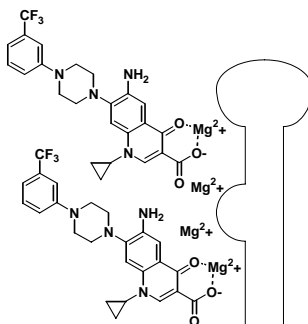


By performing RNA-targeted structure–activity-relationship (SAR) studies, we discovered a novel peptidomimetic containing squaryldiamide as a potential bioisostere replacement for guanidine that binds TAR RNA with high affinity.

Antiviral 6-amino-quinolones: Molecular basis for potency and selectivity

pp 4247–4251

Sara N. Richter, Barbara Gatto, Oriana Tabarrini, Arnaldo Fravolini and Manlio Palumbo*

**Reactions of α -hydroxyethyl radicals with flavonoids of various structures**

pp 4252–4255

I. B. Hryntsevich and O. I. Shadyro*

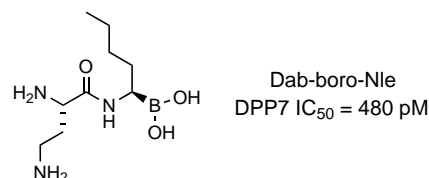
The interaction of α -hydroxyethyl radicals with flavonoids is reported.

Boro-norleucine as a P1 residue for the design of selective and potent DPP7 inhibitors

pp 4256–4260

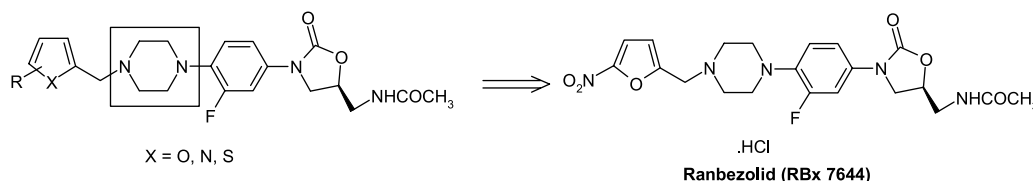
Kevin R. Shreder,* Melissa S. Wong, Sergio Corral, Zhizhou Yu, David T. Winn, Min Wu, Yi Hu, Tyzoon Nomanbhoy, Senaïet Alemayehu, Stacy R. Fuller, Jonathan S. Rosenblum and John W. Kozarich

Dipeptide-based dipeptidyl peptidase inhibitors with C-substituted (alkyl or aminoalkyl) α -amino acids in the P2 position and boro-norleucine (boro-Nle) in the P1 position were synthesized. Dab-boro-Nle (**4g**) proved to be the most selective and potent DPP7 inhibitor with a DPP7 IC₅₀ value of 480 pM.

**Synthesis and SAR of novel oxazolidinones: Discovery of ranbezolid**

pp 4261–4267

Biswajit Das,* Sonali Rudra,* Ajay Yadav, Abhijit Ray, A. V. S. Raja Rao, A. S. S. V. Srinivas, Ajay Soni, Suman Saini, Shalini Shukla, Manisha Pandya, Pragya Bhateja, Sunita Malhotra, Tarun Mathur, S. K. Arora, Ashok Rattan and Anita Mehta

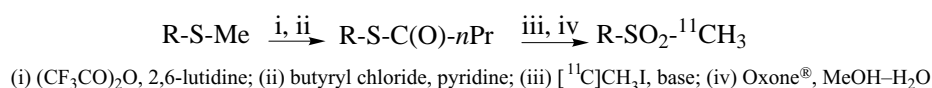


Substitution of five-membered heterocycles on to the 'piperazinyl-phenyl-oxazolidinone' core structure led to the identification of ranbezolid as a clinical candidate. Further replacement of piperazine ring with other diamino-heterocycles led to compounds with potent antibacterial activity.

A general method for the synthesis of aryl [¹¹C]methylsulfones: Potential PET probes for imaging cyclooxygenase-2 expression

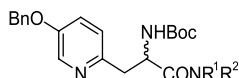
pp 4268–4271

Vattoly J. Majo, Jaya Prabhakaran, Norman R. Simpson, Ronald L. Van Heertum, J. John Mann and J. S. Dileep Kumar*

**Selective cytotoxicity of azatyrosinamides against *ras*-transformed NIH 3T3 cells**

pp 4272–4274

H. P. Wang,* T. L. Hwang, On Lee, Y. J. Tseng, C. Y. Shu and S. J. Lee

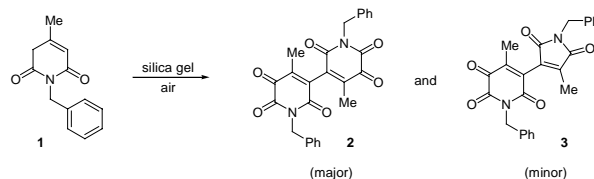


Synthesis and cytotoxicity of novel azatyrosinamides structurally modified from *ras*-specific antioncogenic azatyrosine are reported. Compound **12** (IC₅₀ 16.5 ± 2.2 μM) exhibited selective toxicity on *ras*-transformed NIH 3T3 cells over wild-type cells. The inhibitory activity of this compound was 458-fold higher than that of azatyrosine.

Novel inhibitors of the hepatitis C virus NS3 proteinase

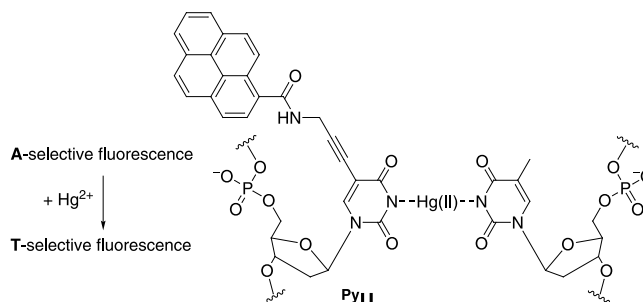
pp 4275–4278

Frank Bennett,* Yi-Tsung Liu, Anil K. Saksena, Ashok Arasappan, Nancy Butkiewicz, Bimalendu Dasmahapatra, John S. Pichardo, F. George Njoroge, Naginbhai M. Patel, Yuhua Huang and Xiaozheng Yang

**Modulation of base selectivity for a base-discriminating fluorescent nucleobase by addition of mercury ion**

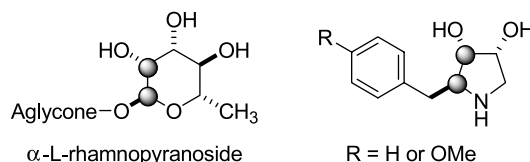
pp 4279–4281

Akimitsu Okamoto,* Yuji Ochi and Isao Saito*

 **α -Rhamnosidase inhibitory activities of polyhydroxylated pyrrolidine**

pp 4282–4285

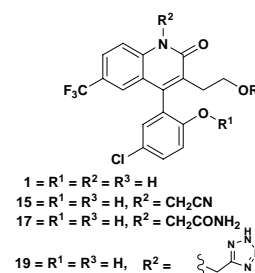
Jin Hyo Kim, Marcus J. Curtis-Long, Woo Duck Seo, Jin Hwan Lee, Byong Won Lee, Yong Jin Yoon, Kyu Young Kang and Ki Hun Park*

**Analogues of a potent maxi-K potassium channel opener with an improved inhibitory profile toward cytochrome P450 isozymes**

pp 4286–4290

Vivekananda M. Vrudhula,* Bireshwar Dasgupta, Christopher G. Boissard, Valentin K. Gribkoff, Kenneth S. Santone, Richard A. Dalterio, Nicholas J. Lodge and John E. Starrett, Jr.*

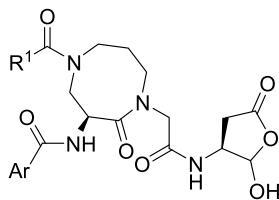
Quinolinone **1** is a potent maxi-K potassium channel opener. In an effort to design analogs of **1** with a better inhibitory profile toward the CYP2C9 isozyme, the two acidic sites were chemically modified independently to generate a number of analogs. These analogs were evaluated as maxi-K channel openers in vitro using *Xenopus laevis* oocytes expressing cloned *hSlo* maxi-K channels. Compounds **15**, **17**, and **19** showed potent activity as maxi-K channel openers and were further evaluated for inhibition of the activity of the CYP2C9 isozyme. Compounds **17** and **19** showed diminished inhibitory potency against 2C9 and also against a panel of other more common CYP isozymes.



Discovery of novel conformationally restricted diazocan peptidomimetics as inhibitors of interleukin-1 β synthesis

pp 4291–4294

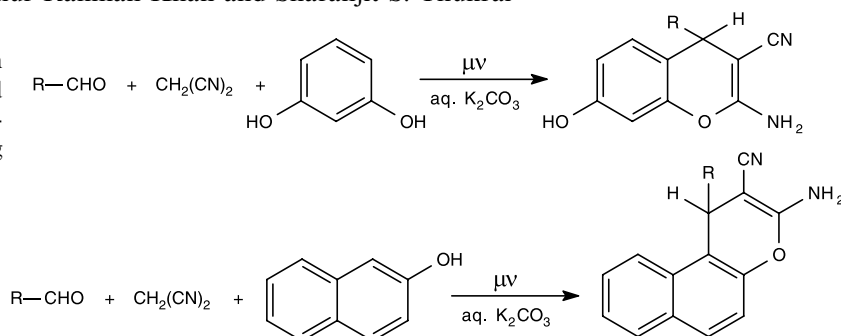
Kofi A. Oppong,* Christopher D. Ellis, Michael C. Laufersweiler, Steven V. O'Neil, Yili Wang, David L. Soper, Mark W. Baize, John A. Vos, Biswanath De, Gregory K. Bosch, Amy N. Fancher, Wei Lu, Maureen K. Suchanek, Richard L. Wang and Thomas P. Demuth, Jr.


Aqua mediated synthesis of substituted 2-amino-4H-chromenes and in vitro study as antibacterial agents

pp 4295–4298

Mazaahir Kidwai,* Shilpi Saxena, M. Khalilur Rahman Khan and Sharanjit S. Thukral

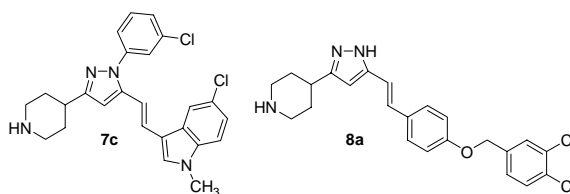
Substituted 2-amino-4H-chromenes have been efficiently synthesized in aqueous K_2CO_3 and their in vitro antibacterial activities were evaluated against standard strains of bacteria using Broth Microdilution MIC method.


Synthesis and antibacterial activity of a novel series of DNA gyrase inhibitors:

pp 4299–4303

5-[(E)-2-arylvinyl]pyrazoles

Akihiko Tanitame,* Yoshihiro Oyamada, Keiko Ofuji, Hideo Terauchi, Motoji Kawasaki, Masaaki Wachi and Jun-ichi Yamagishi

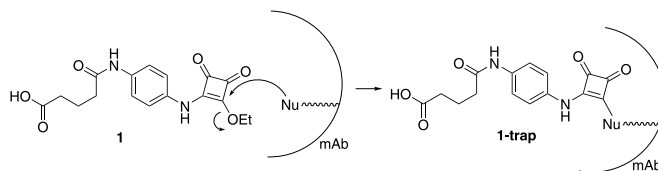


5-[(E)-2-Arylvinyl]pyrazoles **7c** and **8a** exhibited potent antibacterial activity against multidrug resistant Gram-positive bacteria with MIC values equivalent to those against susceptible strains.

Squaric monoamide monoester as a new class of reactive immunization hapten for catalytic antibodies

pp 4304–4307

Yang Xu, Noboru Yamamoto, Diana I. Ruiz, Diane S. Kubitz and Kim D. Janda*

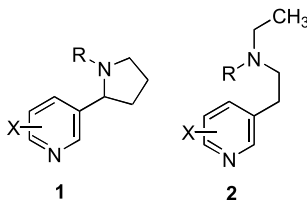


A squaric monoester monoamide motif was employed as an effective reactive immunogen for the discovery of monoclonal antibodies with reactive residue(s) in their combining sites. Two antibodies, 2D4 and 3C8, were uncovered that enhance paraoxon hydrolysis over background. Kinetic analysis of these antibodies was performed and interestingly both undergo a single turnover event due to covalent modification within the antibody combining site. Because antibodies 2D4 and 3C8 result in covalent attachment and thus inactivation of paraoxon, they could be useful probes for investigating paraoxon intoxication.

3-(2-Aminoethyl)pyridine analogs as $\alpha 4\beta 2$ nicotinic cholinergic receptor ligands

pp 4308–4312

Małgorzata Dukat, Anna Ramunno, Rita Banzi, M. Imad Damaj,
Billy Martin and Richard A. Glennon*

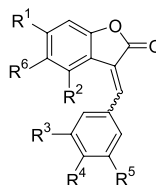


An examination of several 3-(2-aminoethyl)pyridine analogs **2** (with K_i values ranging from 18 to >10,000 nM) and comparison with their structurally related nicotine analogs **1** suggest that the two series likely bind at nicotinic cholinergic receptors in a different fashion.

A new synthesis of isoaurones: Cytotoxic activity of compounds related to the alleged structure of isoaurostatin

pp 4313–4316

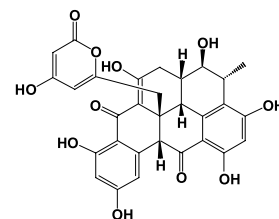
Eleonora Rizzi, Sabrina Dallavalle, Lucio Merlini,* Giovanni Luca Beretta,
Graziella Pratesi and Franco Zunino

**Structural elucidation of A-74528, an inhibitor for 2',5'-phosphodiesterase isolated from *Streptomyces* sp.**

pp 4317–4321

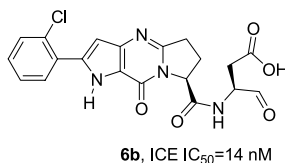
Yoko Fujita, Atsushi Kasuya, Yoichi Matsushita, Miwa Suga, Masaaki Kizuka,
Yasuteru Iijima and Takeshi Ogita*

The structure of A-74528 was elucidated by NMR techniques including natural abundance INADEQUATE to be a highly fused polyketide with a side-chain branching site that never appeared before from the nature. The relative configuration was elucidated by the analyses of NOEs and assessment of dihedral angles predicted by QUANTA/CHARMm computations and coupling constants.

**Synthesis and evaluation of tricyclic pyrrolopyrimidinones as dipeptide mimetics: Inhibition of interleukin-1 β -converting enzyme**

pp 4322–4326

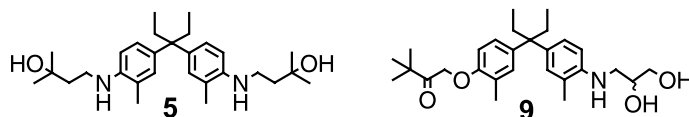
Michael C. Lauferweiler,* Yili Wang, David L. Soper, Maureen K. Suchanek,
Amy N. Fancher, Wei Lu, Richard L. Wang, Kofi A. Oppong, Christopher D. Ellis,
Mark W. Baize, Steven V. O'Neil, John A. Vos and Thomas P. Demuth, Jr.



Ligands with dual vitamin D₃-agonistic and androgen-antagonistic activities

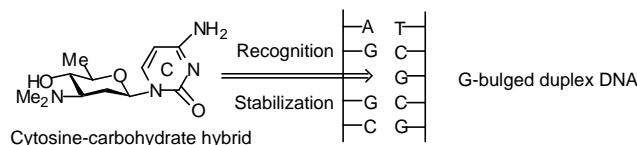
pp 4327–4331

Shinnosuke Hosoda, Aya Tanatani,* Ken-ichi Wakabayashi, Yusuke Nakano, Hiroyuki Miyachi, Kazuo Nagasawa and Yuichi Hashimoto*

**Molecular design, chemical synthesis, and evaluation of cytosine–carbohydrate hybrids for selective recognition of a single guanine bulged duplex DNA**

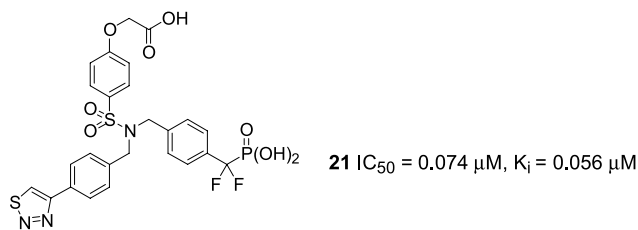
pp 4332–4335

Yusuke Idutsu, Ayaka Sasaki, Shuichi Matsumura and Kazunobu Toshima*

**Discovery and structure–activity relationships of novel sulfonamides as potent PTP1B inhibitors**

pp 4336–4341

Christopher P. Holmes,* Xianfeng Li, Yijun Pan, Caiding Xu, Ashok Bhandari, Claire M. Moody, Joy A. Miguel, Steven W. Ferla, M. Nuria De Francisco, Brian T. Frederick, Siqun Zhou, Natalie Macher, Larry Jang, Jennifer D. Irvine and J. Russell Grove

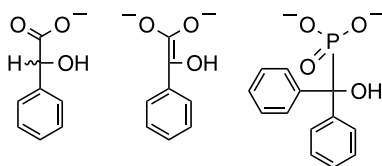


A series of novel sulfonamides containing a single DFMP group were discovered to be potent inhibitors of PTP1B. Investigation of SAR led to the identification of compounds with IC_{50} or K_i values in the low nanomolar range.

Inhibition of mandelate racemase by the substrate–intermediate–product analogue 1,1-diphenyl-1-hydroxymethylphosphonate

pp 4342–4344

Rodney K. M. Burley and Stephen L. Bearne*

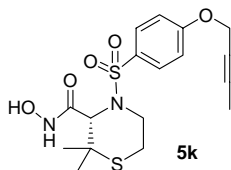


Mandelate racemase has been studied as a paradigm for enzyme-catalyzed abstraction of a proton from carbon acids with relatively high pK_a values. 1,1-Diphenyl-1-hydroxymethylphosphonate is a substrate–intermediate–product analogue and is a modest competitive inhibitor of the enzyme ($K_i = 1.41 \pm 0.09$ mM), suggesting that simultaneous binding of the two phenyl groups obviates mimicry of the *aci*-carboxylate function of the intermediate by the phosphonate group.

Acetylenic TACE inhibitors. Part 2: SAR of six-membered cyclic sulfonamide hydroxamates

pp 4345–4349

J. I. Levin,* J. M. Chen, L. M. Laakso, M. Du, X. Du, A. M. Venkatesan,
V. Sandanayaka, A. Zask, J. Xu, W. Xu, Y. Zhang and J. S. Skotnicki

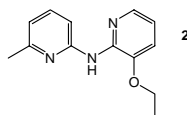


The SAR of a series of potent sulfonamide hydroxamate TACE inhibitors bearing a butynyloxy P1' group was explored. In particular, compound **5k** has excellent in vitro potency against TACE enzyme and in cells, and oral activity in an in vivo model of TNF- α production and a collagen-induced arthritis model.

Dipyridyl amines: Potent metabotropic glutamate subtype 5 receptor antagonists

pp 4350–4353

Theodore M. Kamenecka,* Céline Bonnefous, Steven Govek, Jean-Michel Vernier,
John Hutchinson, Janice Chung, Grace Reyes-Manalo and Jeffery J. Anderson

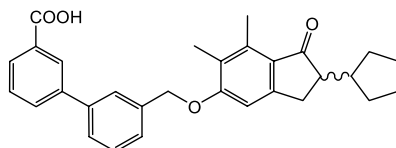


The metabotropic glutamate subtype 5 (mGlu5) receptor has been implicated in a number of CNS disorders. Herein, we report on the discovery, synthesis, and biological evaluation of dipyridyl amines as small molecule mGlu5 antagonists.

Biphenyl-indanones: Allosteric potentiators of the metabotropic glutamate subtype 2 receptor

pp 4354–4358

Céline Bonnefous,* Jean-Michel Vernier, John H. Hutchinson, Michael F. Gardner,
Merryl Cramer, Joyce K. James, Blake A. Rowe, Lorrie P. Daggett,
Hervé Schaffhauser and Theodore M. Kamenecka

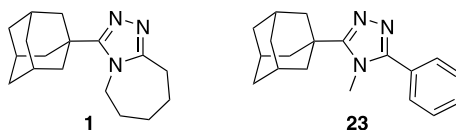


The metabotropic glutamate receptor 2 has been implicated in a number of central nervous system disorders. Herein, we report on the discovery, synthesis, and biological evaluation of biphenyl-indanones as potent small molecule mGluR2 allosteric modulators.

Adamantyl triazoles as selective inhibitors of 11 β -hydroxysteroid dehydrogenase type 1

pp 4359–4362

Steven Olson,* Susan D. Aster, Kai Brown, Linda Carbin, Donald W. Graham,
Anne Hermanowski-Vosatka, Cheryl B. LeGrand, Steven S. Mundt,
Michael A. Robbins, James M. Schaeffer, Llnon H. Slossberg, Michael J. Szymonifka,
Rolf Thieringer, Samuel D. Wright and James M. Balkovec

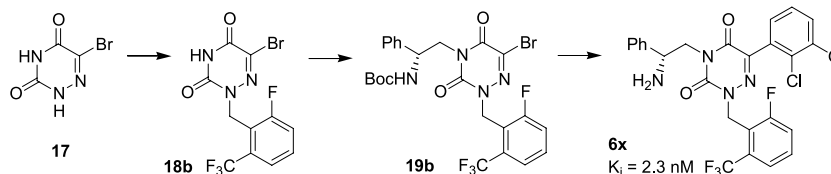


The synthesis and biological activity of selective inhibitors of 11 β -hydroxysteroid dehydrogenase type 1 are reported.

Synthesis of aryl-1,2,4-triazine-3,5-diones as antagonists of the gonadotropin-releasing hormone receptor

pp 4363–4366

Joseph Pontillo, Zhiqiang Guo, Dongpei Wu, R. Scott Struthers and Chen Chen*

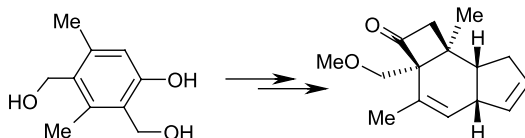


Several efficient synthetic routes for 2-, 4-, and 6-aryl-1,2,4-triazine-3,5-diones were developed. Derivatives were synthesized and studied as gonadotropin-releasing hormone antagonists in an effort to understand structure–activity relationships of the monocyclic compounds.

Molecular complexity from aromatics: Synthesis and photoreaction of *endo*-tricyclo-[5.2.2.0^{2,6}]undecane—A stereoselective route to tricyclic framework of protoilludanes

pp 4367–4369

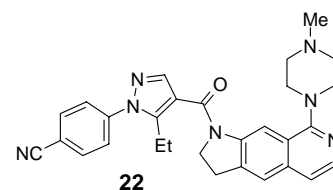
Vishwakarma Singh,* Sanjoy Lahiri and Shantanu Pal



8-Piperazinyl-2,3-dihydropyrrolo[3,2-g]isoquinolines: Potent, selective, orally bioavailable 5-HT₁ receptor ligands

pp 4370–4374

Tom D. Heightman,* Laramie M. Gaster, Sarah L. Pardoe, Jean-Pierre Pilleux, Michael S. Hadley, Derek N. Middlemiss, Gary W. Price, Claire Roberts, Claire M. Scott, Jeannette M. Watson, Laurie J. Gordon, Vicky A. Holland, Jenifer Powles, Graham J. Riley, Tania O. Stean, Brenda K. Trail, Neil Upton, Nigel E. Austin, Andrew D. Ayrton, Tanya Coleman and Leanne Cutler

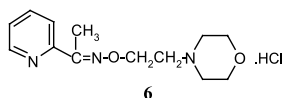


A series of novel 8-piperazinyl-2,3-dihydropyrroloisoquinolines, e.g., compound **22**, was prepared showing high affinity and selectivity for 5-HT_{1A}, 5-HT_{1B} and 5-HT_{1D} receptors combined with favourable pharmacokinetic properties.

Synthesis and antiamoebic activity of new oxime ether derivatives containing 2-acetylpyridine/2-acetylfuran

pp 4375–4379

Mohammad Abid, Kakul Husain and Amir Azam*

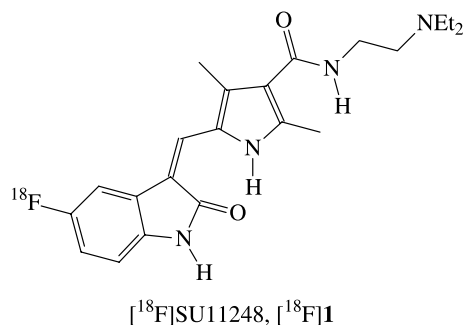


Various oxime ether derivatives of 2-acetylpyridine and 2-acetylfuran series have been synthesised. O-Alkylation of oximes by various alkylaminoethyl halides gave the corresponding oxime ether derivatives. The antiamoebic activities of these compounds were evaluated by microdilution method against *HMI:IMSS* strain of *Entamoeba histolytica*. Four compounds showed lower IC₅₀ values than metronidazole. Moreover, compound **6** showed the most promising antiamoebic activity (IC₅₀ = 0.5 μM vs IC₅₀ = 1.9 μM of metronidazole) in the 2-acetylpyridine series.

Synthesis of [¹⁸F]SU11248, a new potential PET tracer for imaging cancer tyrosine kinase

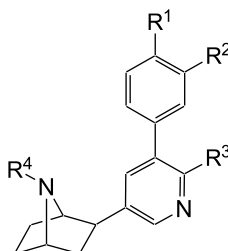
pp 4380–4384

Ji-Quan Wang, Kathy D. Miller, George W. Sledge and Qi-Huang Zheng*

**Epibatidine analogues as selective ligands for the $\alpha_x\beta_2$ -containing subtypes of nicotinic acetylcholine receptors**

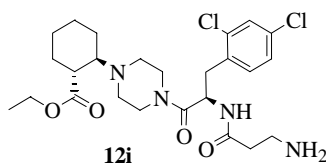
pp 4385–4388

Yiyun Huang,* Zhihong Zhu, Yingxian Xiao and Marc Laruelle

**Potent and orally active non-peptide antagonists of the human melanocortin-4 receptor based on a series of *trans*-2-disubstituted cyclohexylpiperazines**

pp 4389–4395

Fabio C. Tucci,* Nicole S. White, Stacy Markison, Margaret Joppa, Joe A. Tran, Beth A. Fleck, Ajay Madan, Brian P. Dyck, Jessica Parker, Joseph Pontillo, L. Melissa Arellano, Dragan Marinkovic, Wanlong Jiang, Caroline W. Chen, Kathleen R. Gogas, Val S. Goodfellow, John Saunders, Alan C. Foster and Chen Chen*

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*Corresponding author

Supplementary data available via ScienceDirect

COVER

Amerliorating transthyretin amyloidogenesis by native state kinetic stabilization mediated by small molecule binding. Small molecule binding to the amyloidogenic protein transthyretin kinetically stabilizes the native tetrameric state, preventing dissociation to folded monomers that misfold and misassemble into toxic intermediates, amorphous aggregates, and amyloid fibrils. The Kelly laboratory has developed several structurally distinct inhibitor families, depicted in the background, that are undergoing pharmacological evaluation. Created by Steven M. Johnson, graduate student in Professor Jeffery W. Kelly's laboratory, Department of Chemistry, The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA.



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ISSN 0960-894X