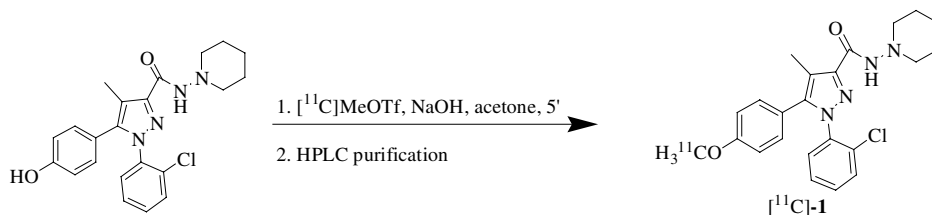


Contents

COMMUNICATIONS

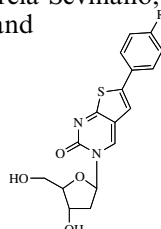
- Synthesis of [*O*-methyl-¹¹C]1-(2-chlorophenyl)-5-(4-methoxyphenyl)-4-methyl-1*H*-pyrazole-3-carboxylic acid piperidin-1-ylamide: a potential PET ligand for CB₁ receptors** pp 2393–2396

J. S. Dileep Kumar,* Jaya Prabhakaran, Victoria Arango, Ramin V. Parsey, Mark D. Underwood, Norman R. Simpson, Suham A. Kassir, Vattoly J. Majo, Ronald L. Van Heertum and J. John Mann



- Bicyclic anti-VZV nucleosides: thieno analogues bearing an alkylphenyl side chain have reduced antiviral activity** pp 2397–2399

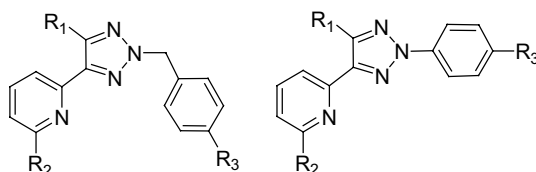
Annette Angell, Christopher McGuigan,* Luis Garcia Sevillano, Robert Snoeck, Graciela Andrei, Erik De Clercq and Jan Balzarini



Thieno analogues of the potent and selective furo-pyrimidine anti-VZV nucleoside family bearing a *p*-alkylphenyl side chain have been synthesised and tested for their antiviral activity against Varicella–Zoster virus (VZV). While the alkyl chain analogues were shown to retain full anti-VZV activity, these new analogues did not when compared to their furo parent nucleosides.

- Synthesis and biological evaluation of novel 2-pyridinyl-[1,2,3]triazoles as inhibitors of transforming growth factor β 1 type 1 receptor** pp 2401–2405

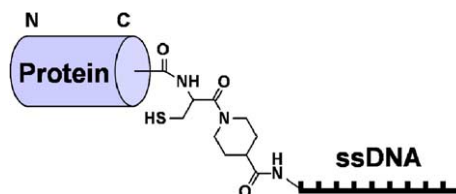
Dae-Kee Kim,* Joonseop Kim and Hyun-Ju Park



Site-specific conjugation of oligonucleotides to the C-terminus of recombinant protein by expressed protein ligation

pp 2407–2410

Shuji Takeda, Shinya Tsukiji and Teruyuki Nagamune*

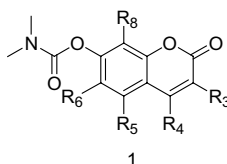


A simple method for conjugating recombinant protein with DNA is reported.

Discovery and structure–activity relationship of coumarin derivatives as TNF- α inhibitors

pp 2411–2415

Jie-Fei Cheng,* Mi Chen, David Wallace, Sovouthy Tith, Thomas Arrhenius, Hirotaka Kashiwagi, Yoshiyuki Ono, Akira Ishikawa, Haruhiko Sato, Toshiro Kozono, Hedeki Sato and Alex M. Nadzan

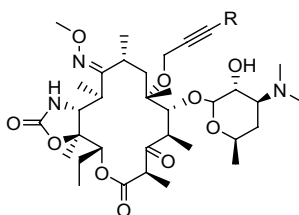


A series of coumarin-based TNF- α inhibitors 1 has been synthesized to establish structure–activity relationship.

Synthesis and antibacterial activity of 6-O-arylpropargyl-9-oxime-11,12-carbamate ketolides

pp 2417–2421

Xenia Beebe,* Fan Yang, Mai H. Bui, Michael J. Mitten, Zhenkun Ma, Angela M. Nilus and Stevan W. Djuric

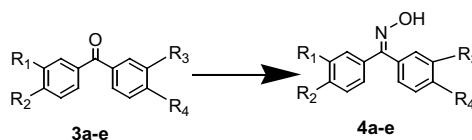


A series of novel 6-O-arylpropargyl-9-oxime-ketolides was synthesized and evaluated against various pathogens. These new compounds show promising in vitro antibacterial potency and in vivo efficacy against macrolide resistant strains.

Synthesis of benzophenone oxime analogues as inhibitor of secretory phospholipase A₂ with anti-inflammatory activity

pp 2423–2425

Satish Kumar Murari, Shimoga Nagaraj Sriharsha, Sheena Shashikanth and Bannikuppe Sannanaik Vishwanath*

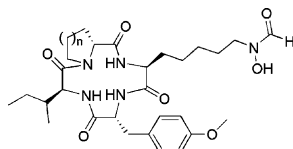


A series of substituted benzophenone oxime analogues has been synthesized and evaluated for in vitro PLA₂ enzyme inhibitory activity and in vivo anti-inflammatory activity using mice.

Synthesis and histone deacetylase inhibitory activity of cyclic tetrapeptides containing a retrohydroxamate as zinc ligand

pp 2427–2431

Norikazu Nishino,* Daisuke Yoshikawa, Louis A. Watanabe, Tamaki Kato, Binoy Jose, Yasuhiko Komatsu, Yuko Sumida and Minoru Yoshida

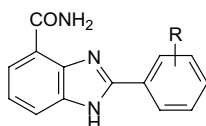


Cyclic tetrapeptide retrohydroxamates were synthesized as HDAC inhibitors with potential as anticancer drugs.

Potential of cytotoxic drug activity in human tumour cell lines, by amine-substituted 2-arylbenzimidazole-4-carboxamide PARP-1 inhibitors

pp 2433–2437

Alex W. White, Nicola J. Curtin, Brian W. Eastman, Bernard T. Golding, Zdenek Hostomsky, Suzanne Kyle, Jianke Li, Karen A. Maegley, Donald J. Skalitzy, Stephen E. Webber, Xiao-Hong Yu and Roger J. Griffin*

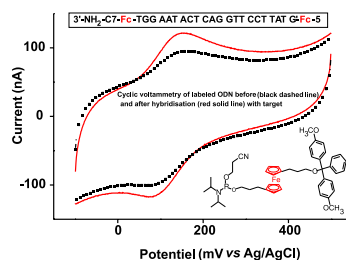


The synthesis and biological evaluation of a new series of amine-substituted 2-arylbenzimidazole-4-carboxamide inhibitors of the DNA-repair enzyme poly(ADP-ribose) polymerase-1 (PARP-1) is reported. The introduction of an amine substituent at the 2-aryl position is not detrimental to activity, with most inhibitors exhibiting K_i values for PARP-1 inhibition in the low nanomolar range. Two compounds in this series were found to potentiate the cytotoxicity of the DNA-methylating agent temozolomide by 4–5-fold in a human colorectal cancer cell line.

Supported synthesis of ferrocene modified oligonucleotides as new electroactive DNA probes

pp 2439–2441

Aude-Emmanuelle Navarro, Nicolas Spinelli, Carole Chaix,* Corinne Moustrou, Bernard Mandrand and Hugues Brisset*

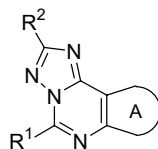


A new type of di-functionalized ferrocene is used directly as reactive synthons for DNA/RNA synthesizer to elaborate electronic DNA probes.

Facile synthesis of fused 1,2,4-triazolo[1,5-c]pyrimidine derivatives as human adenosine A_3 receptor ligands

pp 2443–2446

Takashi Okamura,* Yasuhisa Kurogi, Kinji Hashimoto, Hiroshi Nishikawa and Yoshimitsu Nagao

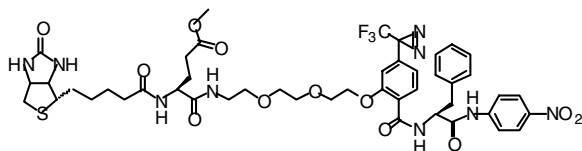


A facile synthetic method for fused triazolopyrimidine derivatives having high affinity and selectivity for human adenosine A_3 receptors is reported.

Enzyme cleavable and biotinylated photoaffinity ligand with diazirine

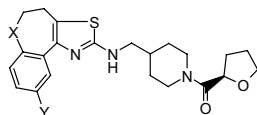
pp 2447–2450

Makoto Hashimoto,* Shun'ji Okamoto, Kensuke Nabeta and Yasumaru Hatanaka

**Discovery and SAR of potent, orally available and brain-penetrable 5,6-dihydro-4*H*-3-thia-1-aza-benzo[*e*]azulen- and 4,5-dihydro-6-oxa-3-thia-1-aza-benzo[*e*]azulen derivatives as neuropeptide Y Y5 receptor antagonists**

pp 2451–2457

Heinrich Rueeger,* Marc Gerspacher, Peter Buehlmayer, Pascal Rigollier, Yasuchika Yamaguchi, Tibur Schmidlin, Steven Whitebread, Barbara Nuesslein-Hildesheim, Hanspeter Nick and Leoluca Cricione

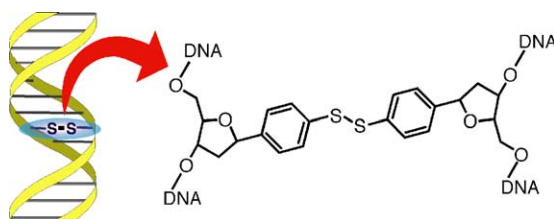


X = CH₂, Y = F hY5 IC₅₀: 2 nM
 X = O, Y = F or Me hY5 IC₅₀: 5 nM

Synthesis and characterization of a DNA analogue stabilized by mercapto C-nucleoside induced disulfide bonding

pp 2459–2462

Akihiko Hatano,* Seiji Makita and Masayuki Kiriara

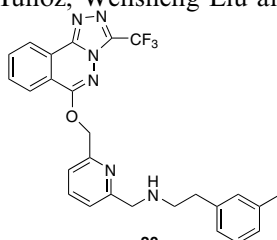


Unnatural mercapto β-C-nucleoside incorporated into DNA. This nucleobase analogue has a reversible redox-active thiol group and formed base pairing with disulfide covalent bonding.

Identification and synthesis of [1,2,4]triazolo[3,4-*a*]phthalazine derivatives as high-affinity ligands to the α₂δ-1 subunit of voltage gated calcium channel

pp 2463–2467

Alec D. Lebsack,* Janet Gunzner, Bowei Wang, Richard Pracitto, Hervé Schaffhauser, Angelina Santini, Jayashree Aiyar, Robert Bezverkov, Benito Munoz, Wensheng Liu and Shankar Venkatraman

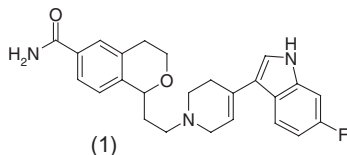


[1,2,4]Triazolo[3,4-*a*]phthalazine derivatives such as **20** (IC₅₀=15 nM) are high-affinity ligands of the α₂δ-1 subunit of voltage gated calcium channel.

SAR development of a selective 5-HT_{1D} antagonist/serotonin reuptake inhibitor lead using rapid parallel synthesis

pp 2469–2472

Graham H. Timms,* John R. Boot, Richard J. Broadmore, Steven L. Carney, Jane Cooper, Jeremy D. Findlay, Jeremy Gilmore, Stephen Mitchell, Nick A. Moore, Ian Pullar, Graham J. Sanger, Rosemary Tomlinson, Beverly B. Tree and Susan Wedley

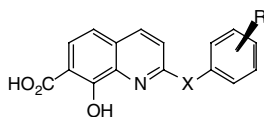


Incorporation of an SRI pharmacophore onto a selective 5-HT_{1D} agonist leads to a molecule having both 5-HT_{1D} antagonist and SRI activity. RPS techniques were employed to identify potential SAR approaches to ameliorating undesired cross-reactivities.

Linker-modified quinoline derivatives targeting HIV-1 integrase: synthesis and biological activity

pp 2473–2476

Christophe Bénard, Fatima Zouhiri, Marie Normand-Bayle, Michèle Danet, Didier Desmaële,* Hervé Leh, Jean-François Mouscadet, Gladys Mbemba, Claire-Marie Thomas, Sabine Bonnenfant, Marc Le Bret and Jean d'Angelo*



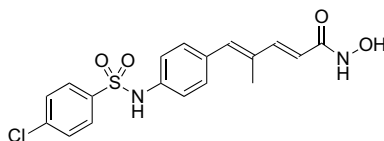
X = CONH, CONHNH, HNCO, NHCONH, COCH=C(OH)

A series of quinoline derivatives linked to an aromatic ring by functionalized spacers was synthesized. The anti-HIV-1 integrase potency was evaluated in both in vitro and ex vivo assays.

Stereodefined and polyunsaturated inhibitors of histone deacetylase based on (2E,4E)-5-arylpenta-2,4-dienoic acid hydroxyamides

pp 2477–2481

Charles M. Marson,* Nawal Serradji, Alphonso S. Rioja, Sebastien P. Gastaud, John P. Alao, R. Charles Coombes and David M. Vigushin

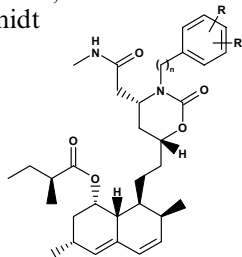


Synthesis and evaluation of unsaturated inhibitors of histone deacetylase are described. Inhibition of histone deacetylase IC₅₀=49 nM.

Statin-derived 1,3-oxazinan-2-ones as submicromolar inhibitors of LFA-1/ICAM-1 interaction: stabilization of the metabolically labile vanillyl side chain

pp 2483–2487

Thomas Ullrich,* Karl Baumann, Karl Welzenbach, Simone Schmutz, Gian Camenisch, Josef G. Meingassner and Gabriele Weitz-Schmidt

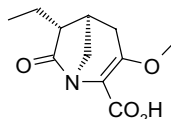


The synthesis, biological activity, and microsomal stability of a series of potent LFA-1/ICAM-1 binding inhibitors of the statin family are presented.

Design and synthesis of bridged γ -lactams as analogues of β -lactam antibiotics

pp 2489–2492

Jozsef Aszodi, David A. Rowlands, Pascale Mauvais, Pascal Collette, Alain Bonnefoy and Maxime Lampilas*

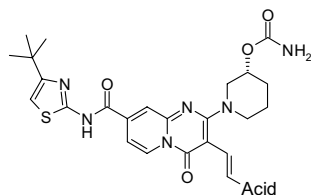


Anti-Bredt bridged bicyclo[3.2.1] γ -lactams were designed as inhibitors of penicillin binding proteins (PBPs). The compounds were prepared by a carbenoid insertion into a lactam N–H bond. Their weak antibacterial activity could either be explained by a poor chemical stability or by unfavorable steric interactions of the methylene bridge of the γ -lactam with the targeted enzymes.

MexAB-OprM specific efflux pump inhibitors in *Pseudomonas aeruginosa*. Part 4: Addressing the problem of poor stability due to photoisomerization of an acrylic acid moiety

pp 2493–2497

Kiyoshi Nakayama,* Noriko Kuru, Masami Ohtsuka, Yoshihiro Yokomizo, Atsunobu Sakamoto, Haruko Kawato, Ken-ichi Yoshida, Toshiharu Ohta, Kazuki Hoshino, Katsuya Akimoto, Junko Itoh, Hiroko Ishida, Aesop Cho, Monica H. Palme, Jason Z. Zhang, Ving J. Lee and William J. Watkins

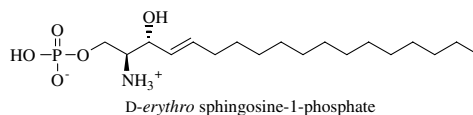


Acid: COOH MPC8: 0.5 μ g/mL
 tetrazole MPC8: <0.25 μ g/mL
 Efflux Pump Inhibitor in *P. aeruginosa*

Syntheses of sphingosine-1-phosphate analogues and their interaction with EDG/S1P receptors

pp 2499–2503

Hyun-Suk Lim, Jeong-Ju Park, Kwangseok Ko, Mee-Hyun Lee and Sung-Kee Chung*

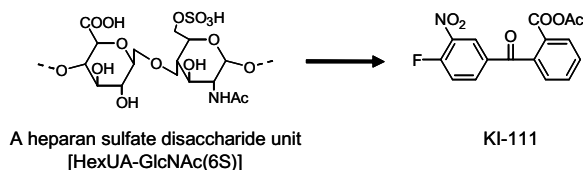


Sphingosine-1-phosphate (S1P) is an important regulator of a wide variety of biological processes acting as an endogenous ligand to EDG/S1P receptors. In an effort to establish structure–activity relationship between EDG/S1P and ligands, we report herein homology modeling study of EDG-1/S1P₁, syntheses of S1P analogues, and cell based binding affinity study for EDG/S1P receptors.

Rational design and synthesis of novel heparan sulfate mimetic compounds as antiadhesive agents

pp 2505–2509

Keisuke Ishida, Siro Simizu, Takayuki Teruya, Michal K. Wierzba and Hiroyuki Osada*

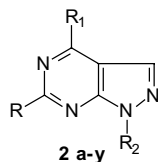


Novel heparan sulfate mimetic compounds (**KI**-compounds) were designed and synthesized as antiadhesive agents.

New pyrazolo[3,4-*d*]pyrimidines endowed with A431 antiproliferative activity and inhibitory properties of Src phosphorylation

pp 2511–2517

S. Schenone,* O. Bruno, A. Ranise, F. Bondavalli, C. Brullo, P. Fossa, L. Mosti, G. Menozzi, F. Carraro, A. Naldini, C. Bernini, F. Manetti and M. Botta

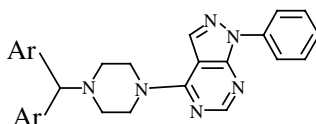


New 4-aminopyrazolo[3,4-*d*]pyrimidines substituted in positions 1 and 6 have been reported. Compounds showed A431 antiproliferative activity and inhibition of Src phosphorylation.

Design, synthesis, and structure–activity relationships of pyrazolo[3,4-*d*]pyrimidines: a novel class of potent enterovirus inhibitors

pp 2519–2525

Jyh-Haur Chern,* Kak-Shan Shia, Tsu-An Hsu, Chia-Liang Tai, Chung-Chi Lee, Yen-Chun Lee, Chih-Shiang Chang, Sung-Nien Tseng and Shin-Ru Shih*

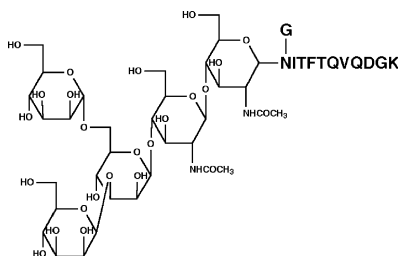


A series of pyrazolo[3,4-*d*]pyrimidines were synthesized and their antiviral activity was evaluated in plaque reduction assay. It is very interesting that this class of compounds provide remarkable evidence that they are very specific for human enteroviruses, in particular, coxsackieviruses.

Structure of pentasaccharide of glycopeptide from TIME-EA4, N-glycoprotein in silkworm diapause eggs

pp 2527–2531

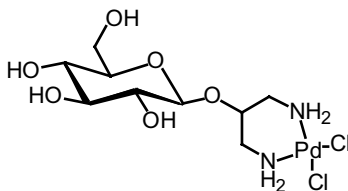
Suthasinee Pitchayawasin, Minoru Isobe,* Naoki Tani and Hidenori Kai



Synthesis, structural characterization, and antitumor activity of palladium(II) complexes containing a sugar unit

pp 2533–2536

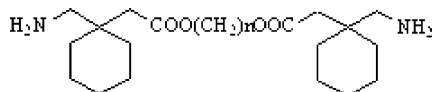
Izabela Brudzińska, Yuji Mikata,* Makoto Obata, Chikara Ohtsuki and Shigenobu Yano*



Effect of gabapentin derivatives on mechanical allodynia-like behaviour in a rat model of chronic sciatic constriction injury

pp 2537–2541

Yang Hong-Ju,* Liu He, Shi Wei-Guo, Zhao Nan, Yuan Wei-Xiu, Jiang Zhong-Wei, Wang Jun-Wei, Gong Zheng-Hua, Zhong Bo-Hua, Luo Zhi-Pu and Gong Zhe-Hui

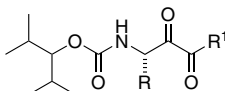


A series of mutual prodrugs were synthesized and their pharmacological properties to treat allodynia were investigated.

Orally bioavailable small molecule ketoamide-based inhibitors of cathepsin K

pp 2543–2546

David G. Barrett, John G. Catalano, David N. Deaton,* Stacey T. Long, Larry R. Miller, Francis X. Tavares, Kevin J. Wells-Knecht, Lois L. Wright and Hui-Qiang Q. Zhou

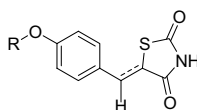


An orally available series of ketoamide-based inhibitors of cathepsin K has been identified. Starting from a potent inhibitor with poor oral bioavailability, modifications to P^I and P^{II} elements led to enhancements in solubility and permeability. These improvements resulted in orally available cathepsin K inhibitors.

Structure–activity requirements for the antiproliferative effect of troglitazone derivatives mediated by depletion of intracellular calcium

pp 2547–2550

Yun-Hua Fan, Han Chen, Amarnath Natarajan, Yuhong Guo, Fred Harbinski, Julia Iyasere, William Christ, Huseyin Aktas and Jose A. Halperin*

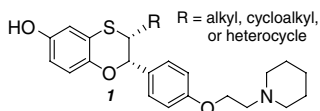


The minimum structural requirements for troglitazone-like compounds to retain their biological activities were reported.

Estrogen receptor ligands. Part 3: The SAR of dihydrobenzoxathiin SERMs

pp 2551–2554

Helen Y. Chen,* Seongkon Kim, Jane Y. Wu, Elizabeth T. Birzin, Wanda Chan, Yi Tien Yang, Johanna Dahllund, Frank DiNinno, Susan P. Rohrer, James M. Schaeffer and Milton L. Hammond

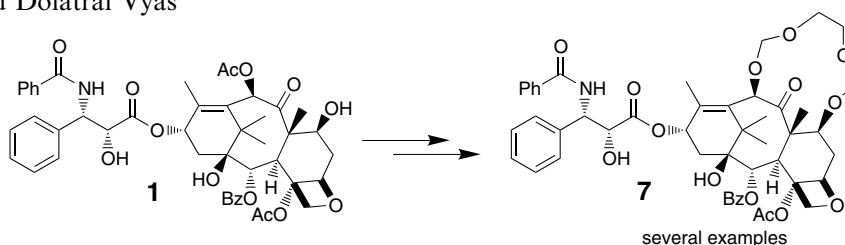


A class of dihydrobenzoxathiins **1** exhibiting a high degree of selectivity for ER α over ER β has been discovered. The SAR of dihydrobenzoxathiins with modifications at the C-3 position is presented.

Synthesis and biological activity of macrocyclic taxane analogues

pp 2555–2558

James G. Tarrant,* Donald Cook, Craig Fairchild, John F. Kadow, Byron H. Long, William C. Rose and Dolatrai Vyas

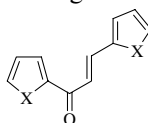


A series of paclitaxel analogues possessing a macrocyclic structure between the 7 and 10 positions has been prepared. These compounds possess in vitro activity against a paclitaxel resistant cell line and have in vivo activity comparable to paclitaxel.

Simple aromatic compounds containing propenone moiety show considerable dual COX/5-LOX inhibitory activities

pp 2559–2562

Yurngdong Jahng, Long-Xuan Zhao, Yoon-Soo Moon, Arjun Basnet, Eun-kyung Kim, Hyeun Wook Chang,* Hye Kyung Ju, Tae Cheon Jeong and Eung-Seok Lee*



X = S, O, CH=CH, CH=N

For the development of safer anti-inflammatory agents, simple aromatic compounds containing propenone moiety were prepared and evaluated for their dual COX/5-LOX inhibitory activities. Among the 17 prepared compounds, most compounds exhibited considerable COX/5-LOX inhibitory activities. Especially compound C₁₅ showed the most significant dual COX/5-LOX inhibitory activities.

A novel 11-residual peptaibol-derived carrier peptide for in vitro oligodeoxynucleotide delivery into cell

pp 2563–2566

Shun-ich Wada* and Reiko Tanaka

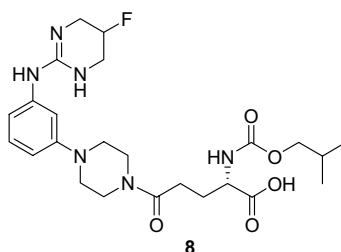
Using a pore- and channel-forming peptide, TV-XIIa, which is an 11-residual peptaibol isolated from the fungus *Trichoderma viride*, we developed a vehicle for cellular delivery of antisense oligodeoxynucleotides (ODNs). The designed carrier peptide is able to translocate ODNs into NIH3T3 cells at both 4 and 37°C, and the translocation does not seem to involve an energy-dependent endocytic process.

Carrier peptide: Ac-U-N-I-I-U-P-L-L-U-P-I-K-K-K-K-K-K-K-K-K-OH (U: α -aminoisobutyric acid)

Discovery of a potent and selective $\alpha_v\beta_3$ integrin antagonist with strong inhibitory activity against neointima formation in rat balloon injury model

pp 2567–2570

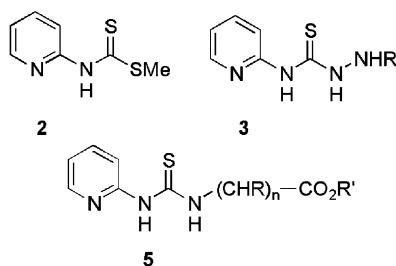
Seiji Iwama,* Tomoko Kitano, Fumiyo Fukuya, Yayoi Honda, Yuji Sato, Mitsue Notake and Toshiya Morie



Synthesis and glucose-6-phosphatase inhibitory activity of (thiouriedo)alkanoic acid esters

pp 2571–2574

Farhanullah, Diptesh Sil, Brajendra K. Tripathi, Arvind K. Srivastava and Vishnu Ji Ram*



Synthesis and glucose-6-phosphatase inhibitory activity of (thiouriedo)alkanoic acid esters are reported.

Peripheral substituents of di(pyridiumyl)porphyrins affected on their interactions with DNA

pp 2575–2577

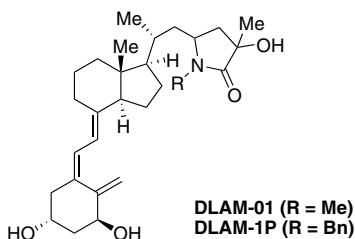
Song Wu, Ping Wang, Tian Tian, Lin Wu, Hanping He, Xiang Zhou,* Xiaolian Zhang* and Xiaoping Cao

meso- and β -Substituted di(pyridiumyl)porphyrins **3**, **4**, and **7** have been synthesized and their interactions with DNA have been investigated. *meso*-Substituted porphyrins showed the stronger effect on DNA than that of β -substituted porphyrin. Cytotoxicity of compound **3** (IC₅₀) to THP-1 tumor cell was up to 0.11 nM.

Synthesis of 1 α ,25-dihydroxyvitamin D₃-26,23-lactams (DLAMs), a novel series of 1 α ,25-dihydroxyvitamin D₃ antagonist

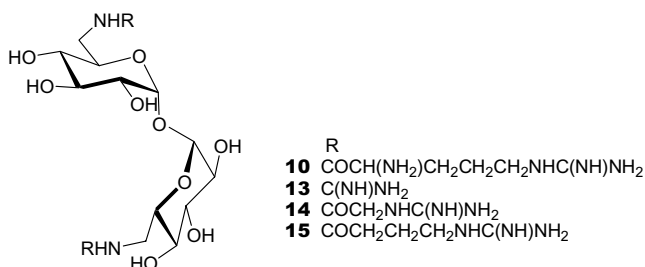
pp 2579–2583

Yuko Kato, Yusuke Nakano, Hiroko Sano, Aya Tanatani, Hisayoshi Kobayashi, Rumiko Shimazawa, Hiroyuki Koshino, Yuichi Hashimoto and Kazuo Nagasawa*

 **α,α -Trehalose derivatives bearing guanidino groups as inhibitors to HIV-1 Tat–TAR RNA interaction in human cells**

pp 2585–2588

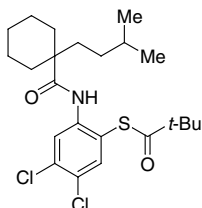
Min Wang, Zhidong Xu, Pengfei Tu, Xiaolin Yu, Sulong Xiao and Ming Yang*



S-(2-(Acylamino)phenyl) 2,2-dimethylpropanethioates as CETP inhibitors

pp 2589–2591

Kimiya Maeda, Hiroshi Okamoto and Hisashi Shinkai*

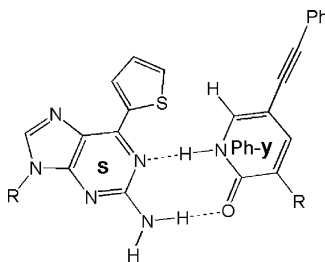


Studies on the relationship between the structure of the benzene moiety of *S*-(2-(acylamino)phenyl) 2,2-dimethylpropanethioates and CETP inhibitory activity were performed. The most potent compound achieved 50% inhibition of CETP activity in human plasma at a concentration of 2 μ M.

Unnatural base pairs mediate the site-specific incorporation of an unnatural hydrophobic component into RNA transcripts

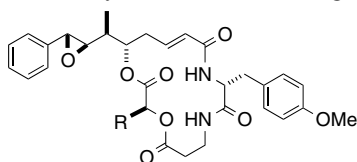
pp 2593–2596

Masayuki Endo, Tsuneo Mitsui, Taeko Okuni, Michiko Kimoto, Ichiro Hirao* and Shigeyuki Yokoyama*

**New analogue of arenastatin A, a potent cytotoxic spongean depsipeptide, with anti-tumor activity**

pp 2597–2601

Nobutoshi Murakami, Satoru Tamura, Kouhei Koyama, Masanori Sugimoto, Ryuji Maekawa and Motomasa Kobayashi*

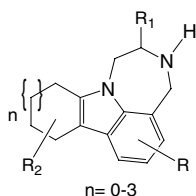
arenastatin A (1): R = CH₂CH(CH₃)₂15-*i*-propylanalogue: R = CH(CH₃)₂15-*t*-butylanalogue: R = C(CH₃)₃

Two analogues possessing steric hindered substituents on C-15 of arenastatin A (1), a potent cytotoxic spongean depsipeptide, were synthesized and shown to enhance the stability in mouse serum. In particular, 15-*tert*-butylanalogue with higher cytotoxicity exhibited anti-tumor activity through iv administration different from 1.

Cycloalkyl[*b*][1,4]benzodiazepinoindoles are agonists at the human 5-HT_{2C} receptor

pp 2603–2607

Annmarie L. Sabb,* Robert L. Vogel, Gregory S. Welmaker, Joan E. Sabalski, Joseph Coupet, John Dunlop, Sharon Rosenzweig-Lipson and Boyd Harrison

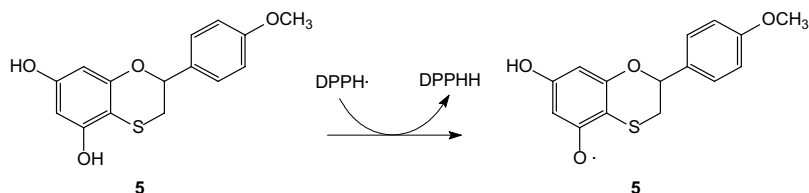


The synthesis and characterization of a new class of human 5-HT_{2C} receptor agonists are described. Potent and selective 5-HT_{2C} receptor agonists have been identified in this class of molecules.

Unexpected role of 5-OH in DPPH radical-scavenging activity of 4-thiaflavans. Revealed by theoretical calculations

pp 2609–2611

Lan-Fen Wang and Hong-Yu Zhang*

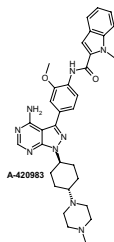


By means of density functional theory calculations, 5-OH in 4-thiaflavans was revealed, unexpectedly, to be more active than 7-OH in scavenging DPPH radical.

A-420983: a potent, orally active inhibitor of I κ B with efficacy in a model of transplant rejection

pp 2613–2616

David W. Borhani, David J. Calderwood,* Michael M. Friedman, Gavin C. Hirst,*
Biqin Li, Adelaine K.W. Leung, Brad McRae, Sheldon Ratnofsky, Kurt Ritter and Wendy Waegell

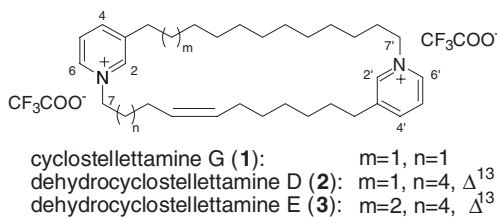


A-420983 (compound 7) is a potent inhibitor of I κ B. A-420983 exhibits oral efficacy in animal models of delayed-type hypersensitivity and organ transplant rejection.

Three new cyclostelletamines, which inhibit histone deacetylase, from a marine sponge of the genus *Xestospongia*

pp 2617–2620

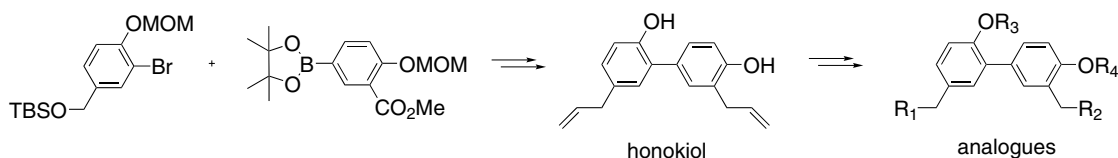
Naoya Oku, Koji Nagai, Nobuaki Shindoh, Yoh Terada, Rob W.M. van Soest, Shigeki Matsunaga and Nobuhiro Fusetani*



Efficient synthesis and structure–activity relationship of honokiol, a neurotrophic biphenyl-type neolignan

pp 2621–2625

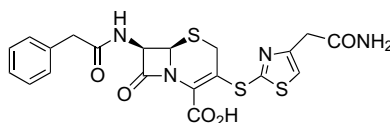
Tomoyuki Esumi, Gouki Makado, Haifeng Zhai, Yasuhiro Shimizu, Yasuhide Mitsumoto and Yoshiyasu Fukuyama*



Honokiol has been synthesized by utilizing Pd-catalyzed Suzuki–Miyaura coupling reaction as a key step. The structure–activity relationship between neurite outgrowth-promoting activity and its O-methylated and/or its hydrogenated analogues in the primary cultures of fetal rat cortical neurons suggests that 5-allyl and 4'-hydroxyl groups are essential for affecting the neurotrophic activity of honokiol.

Studies on anti-*Helicobacter pylori* agents. Part 3: A novel, efficacious cephem derivative, FR193879 pp 2627–2631

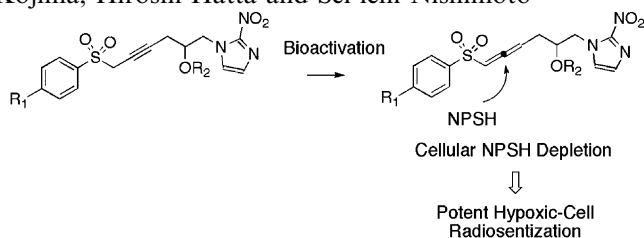
Yoshiki Yoshida,* Keiji Matsuda, Hiroshi Sasaki, Yoshimi Matsumoto, Satoru Matsumoto, Shuichi Tawara and Hisashi Takasugi

**8a (FR193879)**

The synthesis, therapeutic efficacy against *Helicobacter pylori*, and preliminary safety of the novel cephem derivative, FR 193879 (**8a**) are described. Compound **8a** having a (4-carbamoylmethylthiazol-2-yl)thio moiety at the 3-position and a phenylacetamido at the 7-position was found to have good safety showing a nontoxic dose of >100 mg/kg in dogs in a 4-week repeat dose toxicity study and extremely potent therapeutic efficacy against *H. pylori*, showing 30 times superior activity compared to AMPC, and did not display cross-resistance with CAM or MNZ.

Propargylic sulfones possessing a 2-nitroimidazole function: novel hypoxic-cell radiosensitizers with intracellular non-protein thiol depletion ability pp 2633–2635

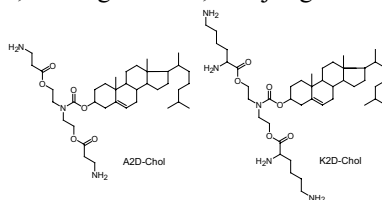
Kazuhito Tanabe,* Ryusuke Kojima, Hiroshi Hatta and Sei-ichi Nishimoto*



Propargylic sulfones containing a 2-nitroimidazole function have been synthesized to evaluate their hypoxic-cell radiosensitizing activity toward EMT6/KU tumor cells and intracellular nonprotein thiol (NPSH) depletion reactivity.

New cationic lipids for gene transfer with high efficiency and low toxicity: T-shape cholesterol ester derivatives pp 2637–2641

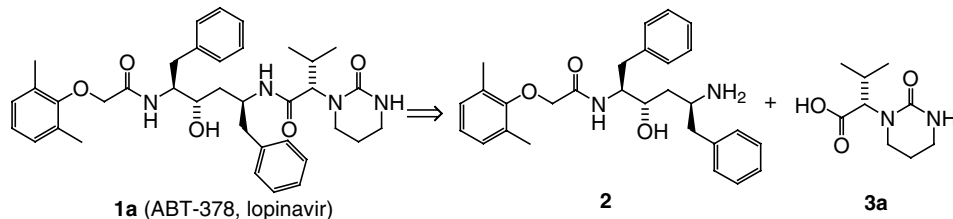
Yan Lee, Heebeom Koo, Yong-beom Lim, Youngeun Lee, Heejung Mo and Jong Sang Park*



New degradable cationic ester lipids with 'T-shape' configurations were synthesized and tested for gene delivery carrier. Their transfection efficiency and toxicity were compared with commercially available cationic lipids, DOTMA, DOSPA, and DC-Chol. They showed efficient transfection activity and almost no toxicity on mammalian cell lines. Their ester bond degradation was monitored by ^1H NMR.

Novel lopinavir analogues incorporating heterocyclic replacements of six-member cyclic urea—synthesis and structure–activity relationships pp 2643–2645

Hing L. Sham,* David A. Betebenner, William Rosenbrook, Thomas Herrin, Ayda Saldivar, Sudhida Vasavanonda, Jacob J. Plattner and Daniel W. Norbeck

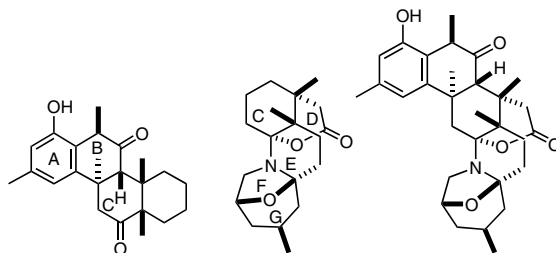
**1a (ABT-378, lopinavir)****2****3a**

The HIV protease inhibitor ABT-378 (lopinavir) has a six-member cyclic urea in the P-2 position. A series of analogues in which the six-member cyclic urea is replaced by various heterocycles was synthesized and the structure–activity relationships explored.

Synthesis and preliminary biological evaluation of truncated zoanthenol analogues

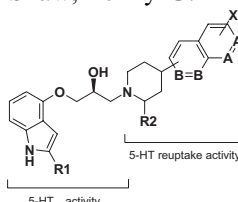
pp 2647–2651

Go Hirai, Hiroki Oguri,* Masahiko Hayashi, Koji Koyama, Yuuki Koizumi, Sameh M. Moharram and Masahiro Hirama*

**Advances toward new antidepressants beyond SSRIs: 1-aryloxy-3-piperidinylpropan-2-ols with dual 5-HT_{1A} receptor antagonism/SSRI activities. Part 4**

pp 2653–2656

Vincent P. Rocco, Patrick G. Spinazze, Todd J. Kohn, Nicholas A. Honigschmidt, David L. Nelson, D. Bradley Wainscott, Laura J. Ahmad, Janice Shaw, Penny G. Threlkeld, David T. Wong and Kumiko Takeuchi*

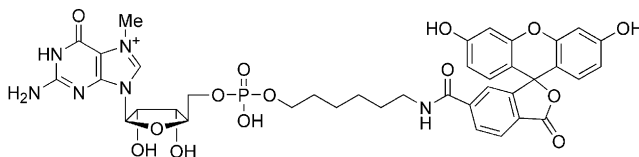


A series of 1-(1*H*-indol-4-yloxy)-3-(4-arylpiperidinyl)propan-2-ols possessing potent dual 5-HT_{1A} receptor antagonism and serotonin reuptake inhibition was discovered. The fused aryl ring moiety contributed to the robust dual activities irrespective of the regiochemistry associated with its connectivity to the piperidine central ring.

Synthesis of fluorescein labeled 7-methylguanosinemonophosphate

pp 2657–2660

Amarnath Natarajan, Nathan Moerke, Yun-Hua Fan, Han Chen, William J. Christ, Gerhard Wagner and Jose A. Halperin*

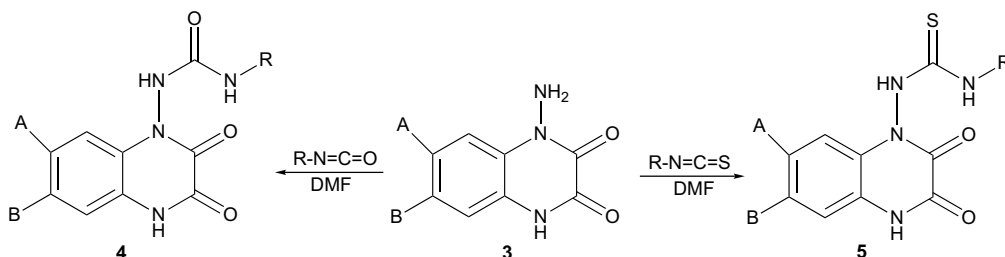


Synthesis of fluorescein labeled 7-methylguanosinemonophosphate.

Lead discovery of quinoxalinediones as an inhibitor of dipeptidyl peptidase-IV (DPP-IV) by high-throughput screening

pp 2661–2664

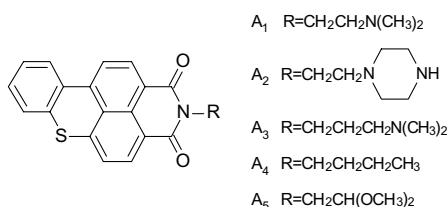
Hyae-Gyeong Cheon, Chul-Min Lee, Beom-Tae Kim and Ki-Jun Hwang*



Highly-efficient DNA photocleavers with long wavelength absorptions: thio-heterocyclic fused naphthalimides containing aminoalkyl side chains

pp 2665–2668

Xuhong Qian,* Yonggang Li, Yufang Xu, Yan Liu and Baoyuan Qu

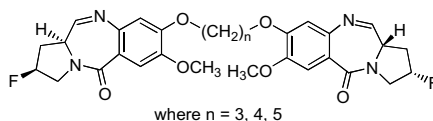


Several photocleavers of thio-heterocyclic fused naphthalimides are designed, synthesized and evaluated.

The effect of C2-fluoro group on the biological activity of DC-81 and its dimers

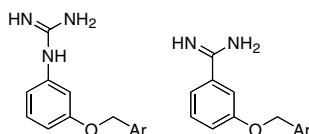
pp 2669–2672

Ahmed Kamal,* P. S. M. M. Reddy and D. Rajasekhar Reddy

**Design, synthesis and evaluation of potential inhibitors of HIV gp120–CD4 interactions**

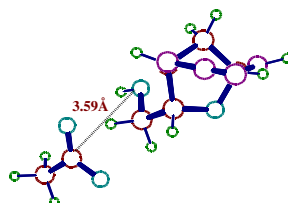
pp 2673–2676

Cyrille Boussard, Thomas Klimkait, Naheed Mahmood, Martin Pritchard and Ian H. Gilbert*

**Threshold interaction energy of NRTI's (2'-deoxy 3'-substituted nucleosidic analogs of reverse transcriptase inhibitors) to undergo competitive inhibition**

pp 2677–2680

Arpita Yadav* and Sanjeev Kumar Singh*

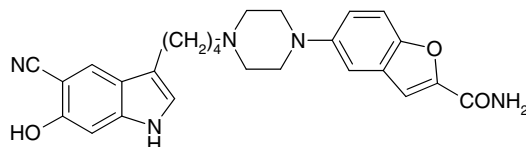


Ab initio Hartree Fock supermolecule calculations (with BSSE) have been carried out to evaluate interaction energies between the drug and the asp 185 of catalytic triad. The study indicates that minor conformational changes may lead to significant differences in interaction energies. The correlation of interaction energies with potency data indicates requirement of ~13 kcal/mol threshold interaction energy for the drug to undergo efficient competitive inhibition.

A new synthesis of indole 5-carboxylic acids and 6-hydroxy-indole-5-carboxylic acids in the preparation of an o-hydroxylated metabolite of vilazodone

pp 2681–2684

Timo Heinrich* and Henning Böttcher

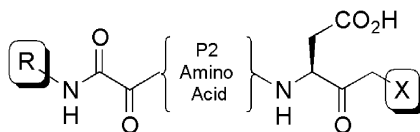


Japp–Klingemann type Fischer-indole synthesis protocols were used to build indole-5-carboxylic acids and derivatives.

Oxamyl dipeptide caspase inhibitors developed for the treatment of stroke

pp 2685–2691

Steven D. Linton,* Teresa Aja, Peter R. Allegrini, Thomas L. Deckwerth, Jose-Luis Diaz, Bastian Hengerer, Julia Herrmann, Kathy G. Jahangiri, Joerg Kallen, Donald S. Karanewsky, Steven P. Meduna, Kip Nalley, Edward D. Robinson, Silvio Roggo, Giorgio Rovelli, Andre Sauter, Robert O. Sayers, Albert Schmitz, Robert Smidt, Robert J. Ternansky, Kevin J. Tomaselli, Brett R. Ullman, Christoph Wiessner and Joe C. Wu



Structural modifications were made to a previously described acyl dipeptide caspase inhibitor, leading to the oxamyl dipeptide series. Subsequent SAR studies directed toward the warhead, P2, and P4 regions of this novel peptidomimetic are described herein.

OTHER CONTENTS

Corrigendum	p 2693
Corrigendum	p 2695
Erratum	p 2697
Contributors to this issue	pp I–III
Instructions to Contributors	pp V–VIII

*Corresponding author

COVER

Cover figure provided by **Indraneel Ghosh**, Department of Chemistry, University of Arizona. The cover depicts the **Dual Surface Selection** methodology developed by the author: the blue helix of htBI (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htBI (center) allows for functional selection against thrombin (right) [Rajagopal, S.; Meza-Romero, R.; Ghosh, I. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1389].



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ISSN 0960-894X