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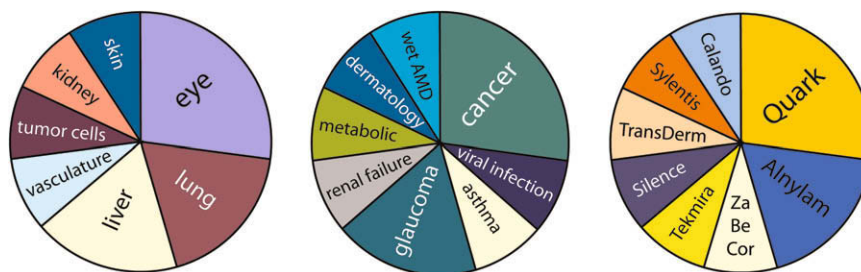
Contents

BMCL DIGEST

Clinical status of duplex RNA

Jonathan K. Watts, David R. Corey*

pp 3203–3207



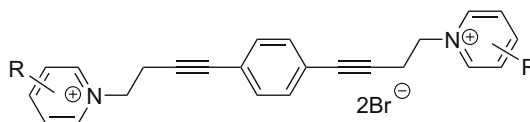
siRNA: having an impact in clinical trials.

REGULAR ARTICLES

Bis-azaaromatic quaternary ammonium salts as ligands for the blood–brain barrier choline transporter

Guangrong Zheng, Zhenfa Zhang, Paul R. Lockman, Werner J. Geldenhuys, David D. Allen, Linda P. Dwoskin, Peter A. Crooks*

pp 3208–3210

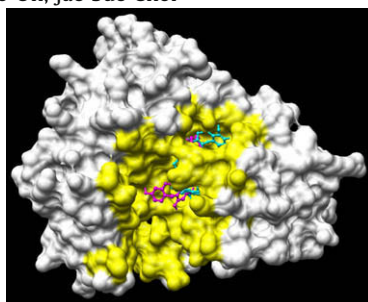


A series of bis-azaaromatic quaternary ammonium compounds containing flexible polymethylene linkers as well as conformationally restricted linkers were evaluated for their affinity for the blood–brain barrier choline transporter (BBB-ChT). The preliminary structure–activity relationships obtained from this study suggest that incorporating a linear, conformationally restricted linker into the molecule improves affinity for the BBB-ChT.

Molecular docking studies of phlorotannins from *Eisenia bicyclis* with BACE1 inhibitory activity

Hyun Ah Jung, Sang Ho Oh, Jae Sue Choi*

pp 3211–3215



Autodockresult : -11.01 Kcal/mol

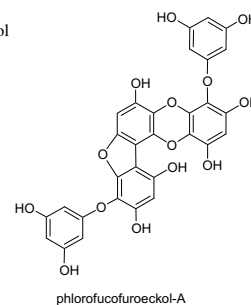
Docking residue :

GLY72, ASP93, SER96, TYR129, PRO131, TYR132, THR133, GLN134, ILE287, ASP289, GLY291, THR293, ASN294

Fred result : -59.5194 Kcal/mol

Docking residue :

GLU73, GLY74, GLY95, VAL130, TYR132, THR133, GLN134, THR259, ILE287, THR292

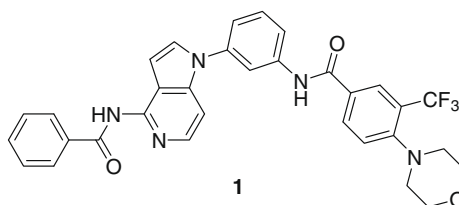


Protein–ligand interactions of phlorofuocoeckol-A ($IC_{50}=2.13\mu M$; $K_i=1.3$) may occur primarily through the TYR132 and THR133 of BACE1 via molecular docking simulations (AUTODOCK 4.0 and FRED 2.0).

Discovery of a new potent bisamide FMS kinase inhibitor

pp 3216–3218

Mohammed I. El-Gamal, Myung-Ho Jung, Chang-Hyun Oh*

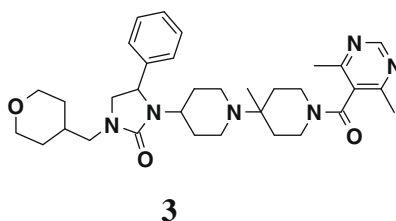


Discovery of a new potent inhibitor of FMS kinase is illustrated. The newly synthesized compound **1** was initially tested at a single concentration of 1 μ M against 47 different kinases. At this concentration, the % inhibitions of the enzymatic activities of FMS and KDR kinases were 90% and 71%, respectively, while the inhibition in activity was less than 58% for all of the other kinases. In addition, the IC_{50} values for compound **1** against FMS and KDR were 96 and 1058 nM, respectively. So, compound **1** was found to be 11 times more selective for FMS kinase than KDR kinase.

Synthesis, SAR and evaluation of [1,4']-bipiperidiny-4-yl-imidazolidin-2-one derivatives as novel CCR5 antagonists

pp 3219–3222

David M. Rotstein*, Stephen D. Gabriel, Nicole Manser, Lubov Filonova, Fernando Padilla, Surya Sankuratri, Changhua Ji, Andre deRosier, Marianna Dioszegi, Gabrielle Heilek, Andreas Jekle, Paul Weller, Pamela Berry

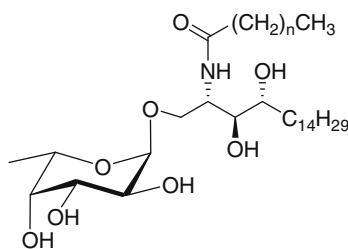


Elaboration of our previously disclosed spiropiperidine template led to the development of a series of novel CCR5 antagonists as represented by analog **3**. Synthetic routes, results of SAR exploration and preliminary lead characterization are described.

Synthesis and biological activity of α -L-fucosyl ceramides, analogues of the potent agonist, α -D-galactosyl ceramide KRN7000

pp 3223–3226

Natacha Veerapen, Faye Reddington, Gabriel Bricard, Steven A. Porcelli, Gurdial S. Besra*

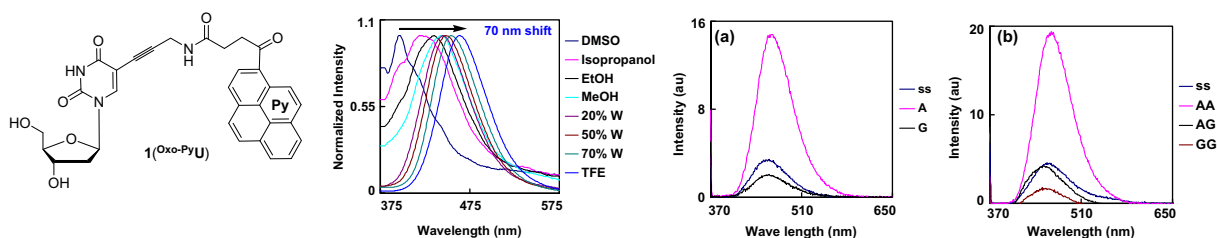


The synthesis of α -L-fucosyl ceramide derivatives and their biological evaluation is described.

Singly and doubly labeled base-discriminating fluorescent oligonucleotide probes containing oxo-pyrene chromophore

pp 3227–3230

Subhendu Sekhar Bag*, Rajen Kundu, Katsuhiko Matsumoto, Yoshio Saito, Isao Saito



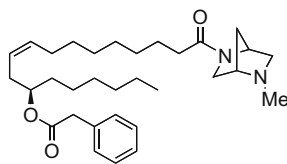
We report the development of new singly and doubly ³Oxo-PyU labeled fluorescent oligonucleotide probes for the discrimination of A and consecutive AA bases of target DNA via generation of enhanced fluorescence signal.



Chemoenzymatic synthesis and cannabinoid activity of a new diazabicyclic amide of phenylacetylricinoleic acid

pp 3231–3234

Manuel López-Ortíz, Andrea Herrera-Solís, Axel Luviano-Jardón, Nidia Reyes-Prieto, Ivan Castillo, Ivan Monsalvo, Patricia Demare, Mónica Méndez-Díaz, Ignacio Regla*, Oscar Prospéro-García*

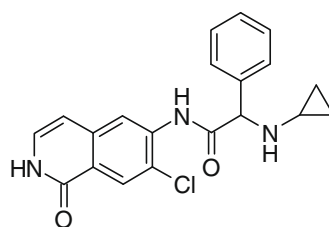
**4** CB1R agonist

The synthesis of a new cannabinoid receptor (CB1R) agonist, derived from ricinoleic acid and a chiral diazabicyclic amide is reported.

Substituted 2H-isoquinolin-1-one as potent Rho-Kinase inhibitors. Part 1: Hit-to-lead account

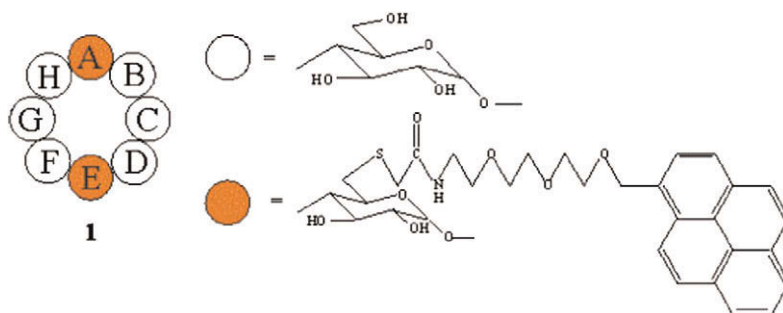
pp 3235–3239

Frank Wu*, Frank H. Büttner, Rhonda Chen, Eugene Hickey, Scott Jakes, Paul Kaplita, Mohammed A. Kashem, Steven Kerr, Stanley Kugler, Zofia Paw, Anthony Prokopowicz, Cheng-Kon Shih, Roger Snow, Erick Young, Charles L. Cywin

**22****Double stranded DNA discrimination by di-pyrene modified γ -cyclodextrin**

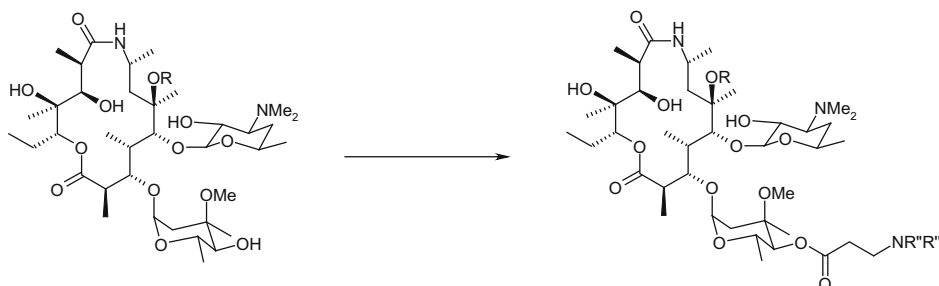
pp 3240–3243

Akane Takeda, Kazuhiko Akimoto, Yoshihiko Kondo, Fumio Hamada*

**Novel 8a-aza-8a-homoerythromycin-4''-(3-substituted-amino)propionates with broad spectrum antibacterial activity**

pp 3244–3249

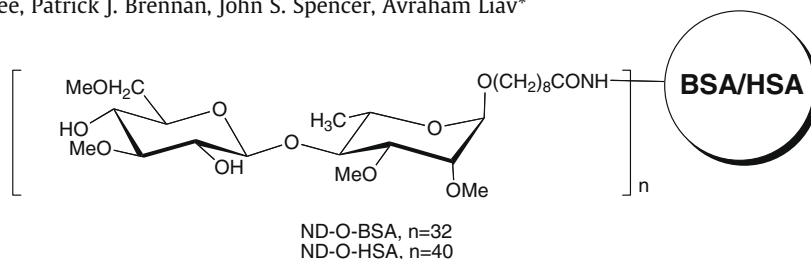
Antun Hutinec*, Marko Đerek, Gorjana Lazarevski, Vitomir Šunjić, Hana Čipčić Paljetak, Sulejman Alihodžić, Vesna Eraković Haber, Miljenko Dumić, Nataša Maršić, Stjepan Mutak



A modified synthesis and serological evaluation of neoglycoproteins containing the natural disaccharide of PGL-I from *Mycobacterium leprae*

pp 3250–3253

Jian Zhang*, Delphi Chatterjee, Patrick J. Brennan, John S. Spencer, Avraham Liav*

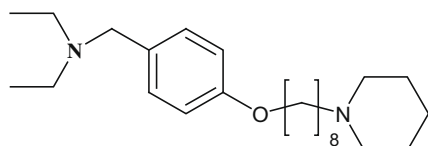


The non-reducing disaccharide segment of phenolic glycolipid I from *Mycobacterium leprae*, O-(3,6-di-O-methyl-β-D-glucopyranosyl)-(1→4)-O-2,3-di-O-methyl-α-L-rhamnopyranose was synthesized by an improved procedure and efficiently conjugated to bovine/human serum albumin.

Synthesis of 4-[(diethylamino)methyl]-phenol derivatives as novel cholinesterase inhibitors with selectivity towards butyrylcholinesterase

pp 3254–3258

Liang Yu, Rihui Cao, Wei Yi, Qin Yan, Zhiyong Chen, Lin Ma, Wenlie Peng*, Huacan Song*



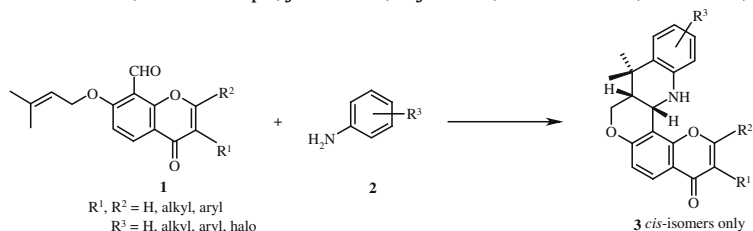
26 IC₅₀=0.092 μM (AChE); IC₅₀=0.0073 μM (BChE)

A series of 4-[(diethylamino)methyl]-phenol derivatives were designed, synthesized, and evaluated as cholinesterase inhibitors. Compound **26** was found to be the most potent inhibitor.

Synthesis of new *cis*-fused tetrahydrochromeno[4,3-*b*]quinolines and their antiproliferative activity studies against MDA-MB-231 and MCF-7 breast cancer cell lines

pp 3259–3264

K. Nagaiah*, A. Venkatesham, R. Srinivasa Rao, V. Saddanapu, J. S. Yadav, S. J. Basha, A. V. S. Sarma, B. Sridhar, A. Addlagatta

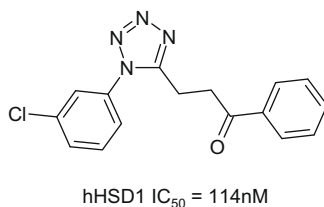


New *cis*-fused tetrahydrochromeno[4,3-*b*]quinolines were synthesized by intramolecular [4+2] imino-Diels–Alder reactions of 2-azadienes derived in situ from aromatic amines and 7-*O*-prenyl derivatives of 8-formyl-2,3-disubstituted chromenones. The structures were established by spectroscopic data and further confirmed by X-ray diffraction analysis. These compounds were evaluated for their antiproliferative activity against MDA-MB-231 and MCF-7 breast cancer cells.

Modulation of 11β-hydroxysteroid dehydrogenase type 1 activity by 1,5-substituted 1*H*-tetrazoles

pp 3265–3271

Scott P. Webster*, Margaret Binnie, Kirsty M. M. McConnell, Karen Sooy, Peter Ward, Michael F. Greaney, Andy Vinter, T. David Pallin, Hazel J. Dyke, Matthew I. A. Gill, Ines Warner, Jonathan R. Seckl, Brian R. Walker

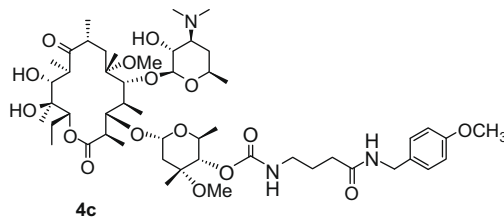


The synthesis and biological activity of a series of 1,5-substituted 1*H*-tetrazoles that modulate 11β-HSD1 activity is reported.

Synthesis and antibacterial activity of novel 4''-O-arylalkylcarbamoyl and 4''-O-((arylalkylamino)-4-oxo-butyl)carbamoyl clarithromycin derivatives

pp 3272–3274

Yongjing Ju, Ruiqing Xian, Ling Zhang, Ruixin Ma, Jichao Cao, Shutao Ma*



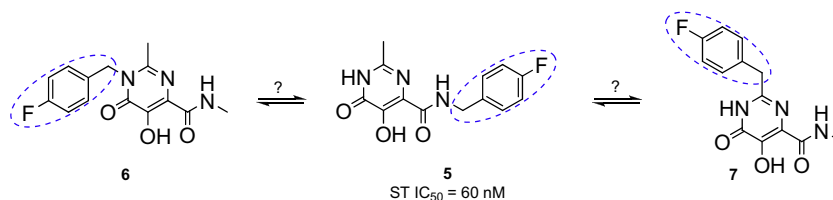
MIC = 0.06 µg/mL

Novel 4''-O-arylalkylcarbamoyl and 4''-O-((arylalkylamino)-4-oxo-butyl)carbamoyl clarithromycin derivatives were designed, synthesized and evaluated for their in vitro antibacterial activities. Among them, compound **4c** was the most effective against *Streptococcus pneumoniae* encoded by the *erm* gene.

**Scaffold rearrangement of dihydroxypyrimidine inhibitors of HIV integrase: Docking model revisited**

pp 3275–3279

Jing Tang, Kasthuraiah Maddali, Yves Pommier, Yuk Y. Sham*, Zhengqiang Wang*

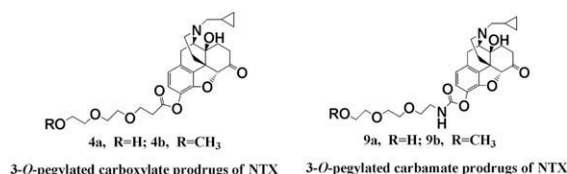


Would benzyl repositioning of known inhibitor **5** create binding difficulties in **6** and **7**?
Existing docking models say **no** and a new model says **yes**.

**Novel 3-O-pegylated carboxylate and 3-O-pegylated carbamate prodrugs of naltrexone for microneedle-enhanced transdermal delivery**

pp 3280–3283

Thirupathi Reddy Yerramreddy, Mikolaj Milewski, Narsimha Reddy Penthala, Audra L. Stinchcomb, Peter A. Crooks*

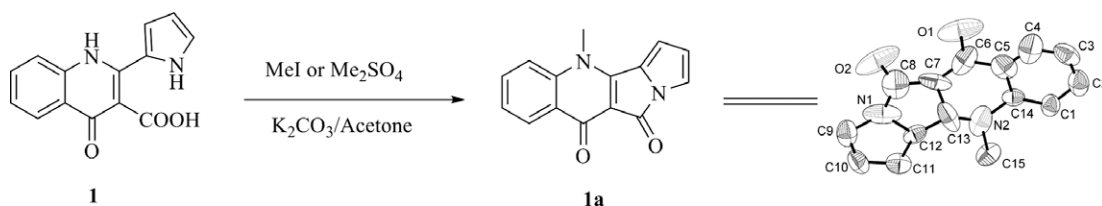


A small library of novel 3-O-pegylated carboxylate prodrugs (**4a–4b**) and 3-O-pegylated carbamate prodrugs (**9a–9b**) of naltrexone were synthesized. The goal behind the design of these prodrugs was to investigate their potential for microneedle-enhanced transdermal delivery. All the synthesized 3-O-pegylated carboxylate prodrugs (**4a–4b**) and 3-O-pegylated carbamate prodrugs (**9a–9b**) of naltrexone were found to have adequate stability in a transdermal formulation and improved apparent solubility compared to naltrexone. Viscosity effects were postulated to be responsible for the observed non-linearity in the flux-concentration profile of these prodrugs.

Penicnoline, a new pyrrolyl 4-quinolinone alkaloid with an unprecedented ring system from an endophytic fungus *Penicillium* sp.

pp 3284–3286

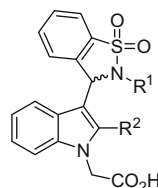
Chang-Lun Shao, Chang-Yun Wang*, Yu-Cheng Gu, Mei-Yan Wei, Jia-Hui Pan, Dong-Sheng Deng, Zhi-Gang She*, Yong-Cheng Lin*



3-Indolyl sultams as selective CRTh2 antagonists

pp 3287–3290

L. Nathan Tumey*, Michael J. Robarge, Elizabeth Gleason, Jianping Song, Steven M. Murphy, George Ekema, Chris Doucette, Doug Hanniford, Marc Palmer, Gary Pawlowski, Joel Danzig, Margaret Loftus, Karen Hunady, Bruce Sherf, Robert W. Mays, Alain Stricker-Krongrad, Kurt R. Brunden, Youssef L. Bennani, John J. Harrington

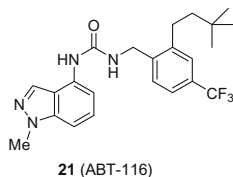


CRTh2 (DP2) is a prostaglandin D2 receptor implicated in the recruitment of eosinophils and basophils within the asthmatic lung. Here we report the discovery of a novel series of 3-indolyl sultams that are low nM antagonists of CRTh2. These compounds proved to be selective over the other primary prostaglandin D2 receptor (DP1) as well as the thromboxane A2 receptor (TP).

Discovery of TRPV1 antagonist ABT-116

pp 3291–3294

Brian S. Brown*, Ryan Keddy, Richard J. Perner, Stanley DiDomenico, John R. Koenig, Tammie K. Jinkerson, Steven M. Hannick, Heath A. McDonald, Bruce R. Bianchi, Prisca Honore, Pamela S. Puttfarcken, Robert B. Moreland, Kennan C. Marsh, Connie R. Faltynek, Chih-Hung Lee

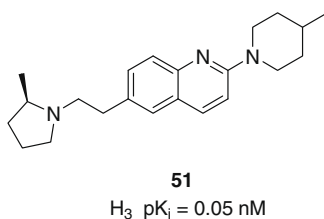


The synthesis and SAR of a series of indazole TRPV1 antagonists leading to the identification of ABT-116 are described.

In vitro studies on a class of quinoline containing histamine H₃ antagonists

pp 3295–3300

Huaqing Liu*, Robert J. Altenbach, Gilbert J. Diaz, Arlene M. Manelli, Ruth L. Martin, Thomas R. Miller, Timothy A. Esbenshade, Jorge D. Brioni, Marlon D. Cowart

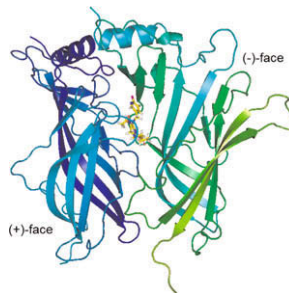


A novel series of histamine H₃ antagonists containing quinoline core was disclosed. Compound **51** showed 50pM affinity for human histamine H₃ in the radio ligand binding assay.

Discovery of bis-aromatic ring neonicotinoid analogues fixed as *cis*-configuration: Synthesis, insecticidal activities, and molecular docking studies

pp 3301–3305

Chuanwen Sun*, Jia Jin, Jun Zhu, Haifeng Wang, Dingrong Yang, Jiahua Xing



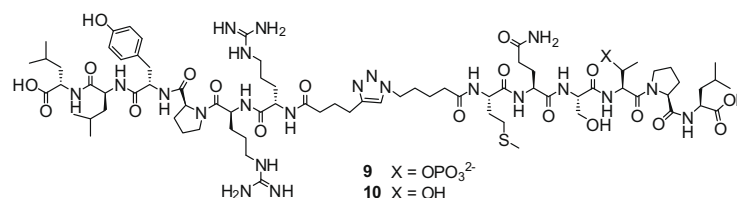
A new series of bis-aromatic ring neonicotinoid analogues (**1a–1l**, **2a–2c**) were prepared and evaluated for their insecticidal activities. Modeling the ligand–receptor complexes by molecular docking explained the structure–activity relationships observed in vitro.



Synthesis of neurotensin(8–13)–phosphopeptide heterodimers via click chemistry

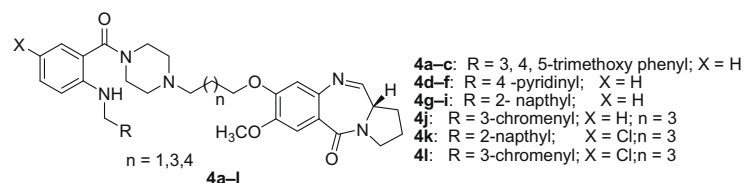
pp 3306–3309

Susan Richter, Theres Ramenda, Ralf Bergmann, T. Kniess, Joerg Steinbach, Jens Pietzsch, Frank Wuest*

**Synthesis, anticancer activity and apoptosis inducing ability of anthranilamide-PBD conjugates**

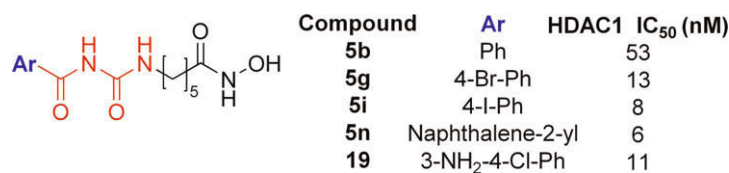
pp 3310–3313

Ahmed Kamal*, E. Vijaya Bharathi, M. Janaki Ramaiah, J. Surendranadha Reddy, D. Dastagiri, A. Viswanath, Farheen Sultana, S. N. C. V. L. Pushpavalli, Manika Pal-Bhadra*, Aarti Juvekar, Subrata Sen, Surekha Zingde

**Acylurea connected straight chain hydroxamates as novel histone deacetylase inhibitors: Synthesis, SAR, and in vivo antitumor activity**

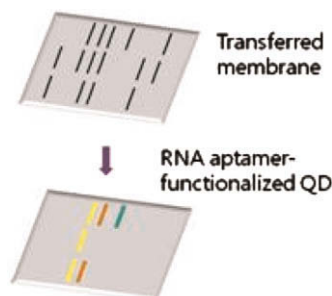
pp 3314–3321

Haishan Wang*, Ze-Yi Lim, Yan Zhou, Melvin Ng, Ting Lu, Ken Lee, Kanda Sangthongpitag, Kee Chuan Goh, Xukun Wang, Xiaofeng Wu, Hwee Hoon Khng, Siok Kun Goh, Wai Chung Ong, Zahid Bonday, Eric T. Sun

**An alternative to Western blot analysis using RNA aptamer-functionalized quantum dots**

pp 3322–3325

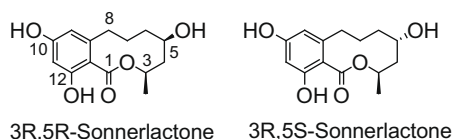
Seonmi Shin, Il-Hyun Kim, Wonchull Kang, Jin Kuk Yang, Sang Soo Hah*



The metabolites of mangrove endophytic fungus Zh6-B1 from the South China Sea

pp 3326–3328

Kai-Kai Li, Yong-Jun Lu, Xiao-Hong Song*, Zhi-Gang She, Xi-Wei Wu, Lin-Kun An, Chuang-Xing Ye, Yong-Cheng Lin*

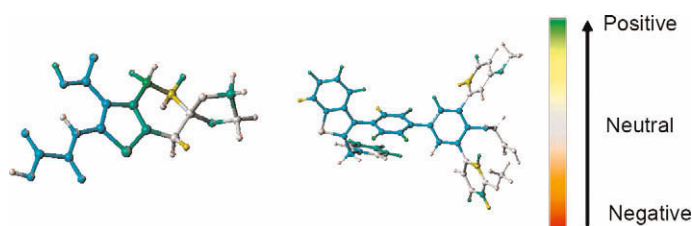


Two new metabolites, 3R,5R-Sonnerlactone and 3R,5S-Sonnerlactone, were isolated from the mangrove endophytic fungus Zh6-B1 from the South China Sea. The absolute configuration of 3R,5R-Sonnerlactone was confirmed by single-crystal X-ray analysis.

Studies on two types of PTP1B inhibitors for the treatment of type 2 diabetes: Hologram QSAR for OBA and BBB analogues

pp 3329–3337

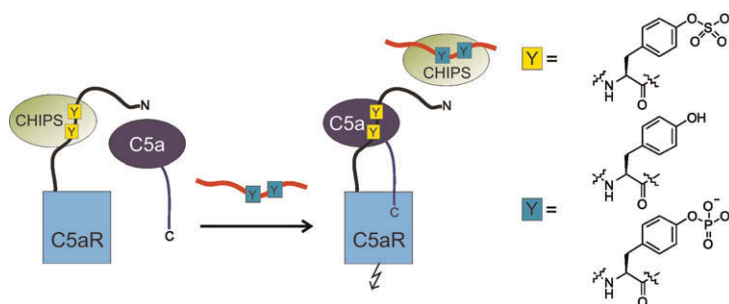
Yuanhua Cheng, Mei Zhou, Chen-Ho Tung, Mingjuan Ji*, Fushi Zhang*



CHIPS binds to the phosphorylated N-terminus of the C5a-receptor

pp 3338–3340

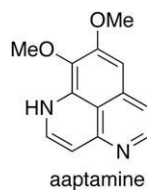
Anton Bunschoten, Louris J. Feitsma, John A. W. Kruijtzter, Carla J. C. de Haas, Rob M. J. Liskamp, Johan Kemmink*



Aptamine, an alkaloid from the sponge *Aaptos suberitoides*, functions as a proteasome inhibitor

pp 3341–3343

Sachiko Tsukamoto*, Rumi Yamanokuchi, Makiko Yoshitomi, Kohei Sato, Tsuyoshi Ikeda, Henki Rotinsulu, Remy E. P. Mangindaan, Nicole J. de Voogd, Rob W. M. van Soest, Hideyoshi Yokosawa

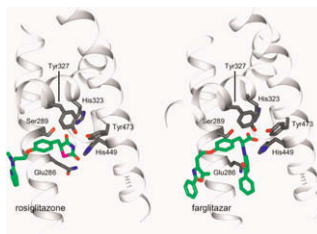


Aptamine, isoaaptamine, and demethylaaptamine were isolated from the marine sponge *Aaptos suberitoides* as proteasome inhibitors. They inhibited the chymotrypsin-like activity of the proteasome with IC₅₀ values of 1.6–4.3 µg/mL.

Flexible ligand recognition of peroxisome proliferator-activated receptor- γ (PPAR γ)

pp 3344–3347

Kenji Yamagishi, Keiko Yamamoto, Yuji Mochizuki, Tatsuya Nakano, Sachiko Yamada, Hiroaki Tokiwa*

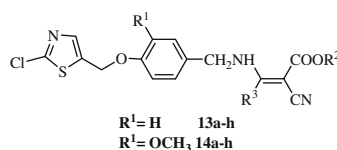


The large LBP of PPAR γ permits different binding systems for typical ligands, and the development of novel ligands of sufficient binding affinity will require adequately hydrophobic pharmacophores.

Synthesis and herbicidal activities of 2-cyano-3-benzylaminoacrylates containing thiazole moiety

pp 3348–3351

Tingting Wang, Guifang Bing, Xin Zhang, Zhenfang Qin, Haibo Yu, Xue Qin, Hong Dai, Wenke Miao, Shanshan Wu, Jianxin Fang*

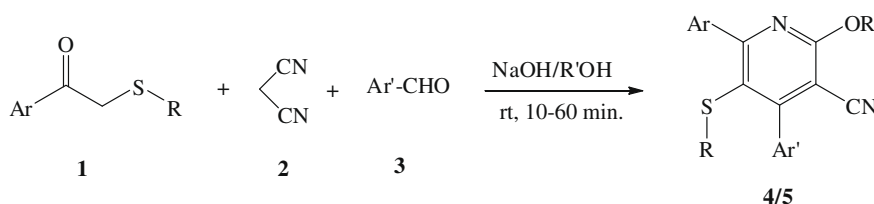


Two series of novel 2-cyano-3-benzylaminoacrylates containing thiazole ring moiety with high Hill inhibitory activities and herbicidal activities were reported.

**Selective one-pot multicomponent synthesis and anti-tubercular evaluation of 5-(aryl/cyclohexylsulfanyl)-2-alkoxy-4,6-diarylpyridine-3-carbonitriles**

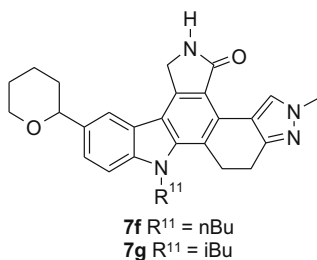
pp 3352–3355

Ramaiyan Manikannan, Shanmugam Muthusubramanian*, Perumal Yogeeswari, Dharmarajan Sriram

**8-THP-DHI analogs as potent Type I dual TIE-2/VEGF-R2 receptor tyrosine kinase inhibitors**

pp 3356–3360

Robert L. Hudkins*, Allison L. Zulli, Ted L. Underiner, Thelma S. Angeles, Lisa D. Aimone, Sheryl L. Meyer, Daniel Pauletti, Hong Chang, Elena V. Fedorov, Steven C. Almo, Alexander A. Fedorov, Bruce A. Ruggeri



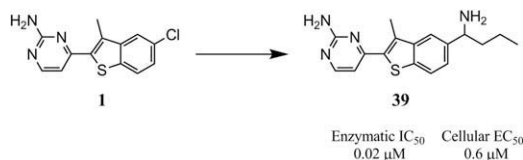
Structure–activity relationships, X-ray crystallography and oral in vivo anti-tumor activity for a series of 8-THP-DHI dual TIE-2/VEGF-R2 inhibitors are reported.



Benzothiophene containing Rho kinase inhibitors: Efficacy in an animal model of glaucoma

pp 3361–3366

Robert L. Davis*, Mehmet Kahraman, Thomas J. Prins, Yan Beaver, Travis G. Cook, Jessica Cramp, Charmagne S. Cayan, Elisabeth M. M. Gardiner, Marsha A. McLaughlin, Abbot F. Clark, Mark R. Hellberg, Andrew K. Shiau, Stewart A. Noble, Allen J. Borchardt

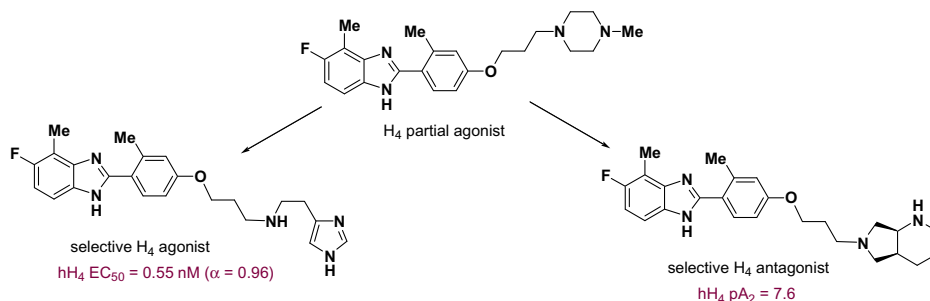


A benzothiophene containing Rho kinase inhibitor was identified in an ultra high-throughput enzymatic assay. SAR studies led to inhibitors with low nM enzymatic IC_{50} s, low or sub- μM cellular EC_{50} s in a novel label-free assay, and in vivo efficacy in a monkey model of ocular hypertension.

Agonist/antagonist modulation in a series of 2-aryl benzimidazole H_4 receptor ligands

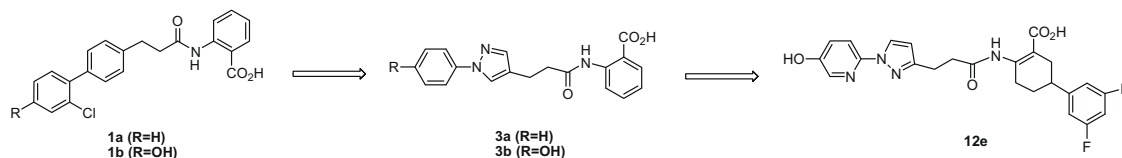
pp 3367–3371

Brad M. Savall*, James P. Edwards, Jennifer D. Venable, Daniel J. Buzard, Robin Thurmond, Michael Hack, Patricia McGovern

**Discovery of pyrazolyl propionyl cyclohexenamide derivatives as full agonists for the high affinity niacin receptor GPR109A**

pp 3372–3375

Fa-Xiang Ding*, Hong C. Shen*, Larrisa C. Wilsie, Mihajlo L. Krsmanovic, Andrew K. Taggart, Ning Ren, Tian-Quan Cai, Junying Wang, Xinchun Tong, Tom G. Holt, Qing Chen, M. Gerard Waters, Milton L. Hammond, James R. Tata, Steven L. Colletti

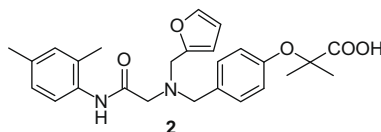


A series of pyrazolyl propionyl cyclohexenamides were discovered as full agonists for the high affinity niacin receptor GPR109A. The structure–activity relationship (SAR) studies were aimed to improve activity on GPR109A, reduce Cytochrome P450 2C8 (CYP2C8) and Cytochrome P450 2C9 (CYP2C9) inhibition, reduce serum shift and improve pharmacokinetic (PK) profiles.

Glycine amides as PPAR α agonists

pp 3376–3379

Klaus Urbahns*, Michael Woltering, Susanne Nikolic, Josef Pernerstorfer, Hilmar Bischoff, Elke Dittrich-Wengenroth, Klemens Lustig

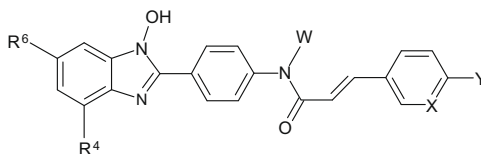


The design, synthesis and pharmacological properties of a novel class of PPAR α agonists is described. Compound **2** is a novel, potent and specific glycine amide with oral bioavailability in rodents. The compound is active in vivo and alters plasma lipids in hAPO-A1 transgenic mice after oral administration.

N-Hydroxybenzimidazole inhibitors of ExsA MAR transcription factor in *Pseudomonas aeruginosa*: In vitro anti-virulence activity and metabolic stability

pp 3380–3383

Mark C. Grier, Lynne K. Garrity-Ryan, Victoria J. Bartlett, Kevin A. Klausner, Peter J. Donovan, Caroline Dudley, Michael N. Alekshun, S. Ken Tanaka, Michael P. Draper, Stuart B. Levy, Oak K. Kim*

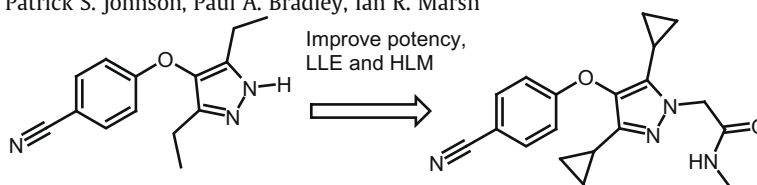


Inhibitors for ExsA-DNA binding in *Pseudomonas aeruginosa*.

**Optimisation of a pyrazole series of progesterone antagonists; Part 1**

pp 3384–3386

Kevin N. Dack*, Sarah Skerratt, Patrick S. Johnson, Paul A. Bradley, Ian R. Marsh



4, HTS hit
PR IC₅₀ 224 nM
LLE 3.3
HLM Cl_{int} 26 μ L/min/mg

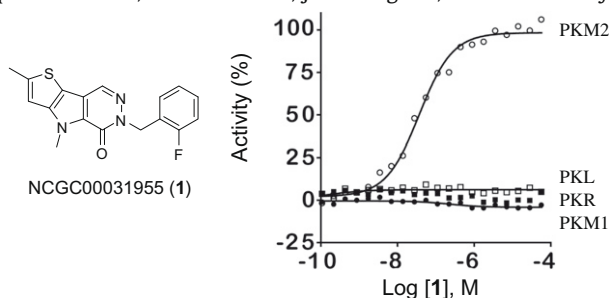
15, PF-02367982
PR IC₅₀ 47 nM
LLE 4.8
HLM Cl_{int} <10 μ L/min/mg

The design and synthesis of a novel series of non-steroidal progesterone receptor antagonists is described. Ligand-lipophilicity efficiency (LLE) was used in the selection of a prototype agent for in vivo pharmacology studies.

Evaluation of thieno[3,2-*b*]pyrrole[3,2-*d*]pyridazinones as activators of the tumor cell specific M2 isoform of pyruvate kinase

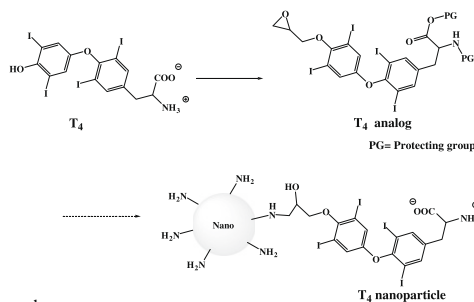
pp 3387–3393

Jian-kang Jiang, Matthew B. Boxer, Matthew G. Vander Heiden, Min Shen, Amanda P. Skoumbourdis, Noel Southall, Henrike Veith, William Leister, Christopher P. Austin, Hee Won Park, James Inglese, Lewis C. Cantley, Douglas S. Auld, Craig J. Thomas*

**Semisynthesis and pharmacological activities of thyroxine analogs: Development of new angiogenesis modulators**

pp 3394–3398

Alexandre Bridoux, Huadong Cui, Evgeny Dyskin, Andreea-Ruxandra Schmitzer, Murat Yalcin, Shaker A. Mousa*



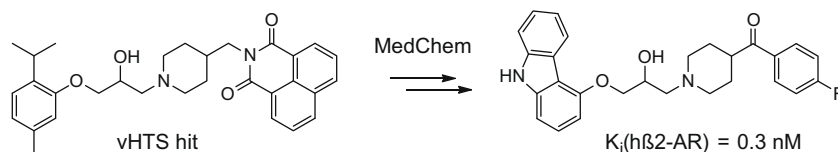
Pharmacological activities of powerful T₄ analogs were found.



A vHTS approach for the identification of β -adrenoceptor ligands

pp 3399–3404

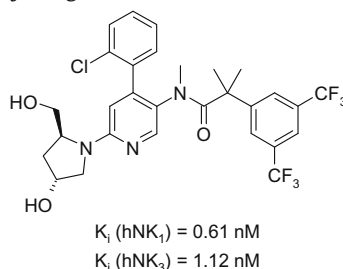
Stefan Tasler*, Roland Baumgartner, Andrea Aschenbrenner, Astrid Ammendola, Kristina Wolf, Tanja Wieber, Josef Schachtner, Marcus Blisse, Udo Quotschalla, Peter Ney



Discovery of potent, balanced and orally active dual NK_1/NK_3 receptor ligands

pp 3405–3408

Jens-Uwe Peters*, Torsten Hoffmann, Patrick Schnider, Heinz Stadler, Andreas Koblet, André Alker, Sonia Maria Poli, Theresa M. Ballard, Will Spooren, Lucinda Steward, Andrew J. Sleight

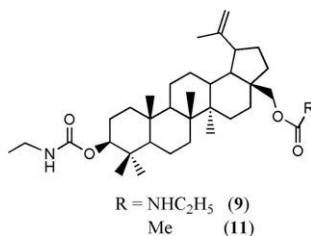


The lead finding activities for a dual NK_1/NK_3 receptor antagonist discovery program, resulting in lead compounds with favourable pharmacological and pharmacokinetic properties, are described.

Carbamate derivatives of betulinic acid and betulin with selective cytotoxic activity

pp 3409–3412

Harish Kommera, Goran N. Kaluderović, Sebastian Dittrich, Jutta Kalbitz, Birgit Dräger, Thomas Mueller, Reinhard Paschke*



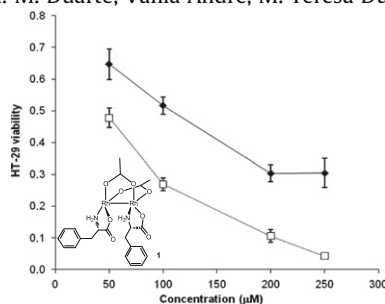
Carbamate derivatives of betulinic acid and betulin were synthesized and tested against fifteen tumor cell lines. The most active compounds **9** (bis(ethylcarbamate)betulin) and **11** (3-O-ethylcarbamate of 28-O-acetylbetulin) were found to be selectively cytotoxic towards tumor cell lines, inducing apoptosis by activation of caspase 3.



New dirhodium complex with activity towards colorectal cancer

pp 3413–3415

Raquel F. M. Frade*, Nuno R. Candeias, Catarina M. M. Duarte, Vânia André, M. Teresa Duarte, Pedro M. P. Gois, Carlos A. M. Afonso*



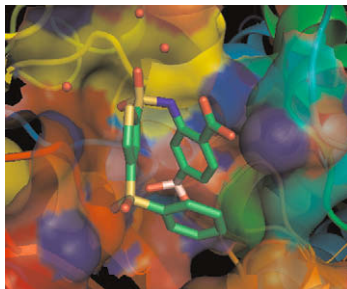
A new rhodium complex ($\text{Rh}_2(\text{L-PheAla})_2(\text{OAc})_2$ **1** has demonstrated a stronger anti-proliferative activity than cisplatin, against a human colon adenocarcinoma cell line.



Structural study of phenyl boronic acid derivatives as AmpC β -lactamase inhibitors

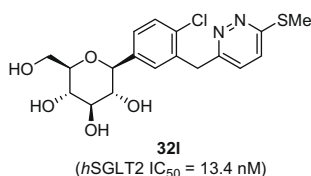
pp 3416–3419

Donatella Tondi*, Samuele Calò, Brian K. Shoichet, Maria Paola Costi*

**Novel C-aryl glucoside SGLT2 inhibitors as potential antidiabetic agents: Pyridazinylmethylphenyl glucoside congeners**

pp 3420–3425

Min Ju Kim, Junwon Lee, Suk Youn Kang, Sung-Han Lee, Eun-Jung Son, Myung Eun Jung, Suk Ho Lee, Kwang-Seop Song, MinWoo Lee, Ho-Kyun Han, Jeongmin Kim, Jinhwa Lee*

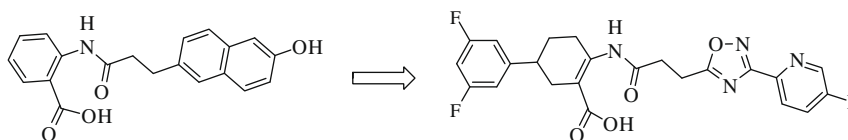


Novel C-aryl glucoside SGLT2 inhibitors containing pyridazine motif were designed and synthesized for biological evaluation. Among various analogs, methylthio-pyridazine **321** demonstrated the best in vitro inhibitory activity against *h*SGLT2 in this series to date (IC₅₀=13.4 nM).

**Anthranilic acid replacements in a niacin receptor agonist**

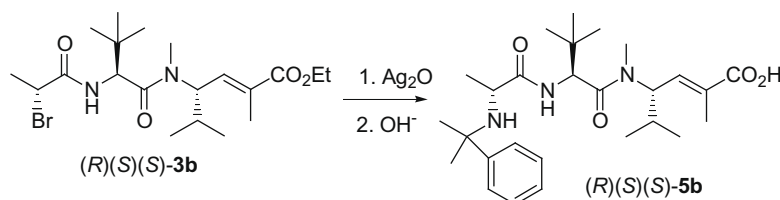
pp 3426–3430

Darby Schmidt*, Abigail Smenton, Subharekha Raghavan, Hong Shen, Fa-Xiang Ding, Ester Carballo-Jane, Silvi Luell, Tanya Ciecko, Tom G. Holt, Michael Wolff, Andrew Taggart, Larissa Wilsie, Mihajlo Krsmanovic, Ning Ren, Daniel Blom, Kang Cheng, Peggy E. McCann, M. Gerard Waters, James Tata, Steven Colletti

**Versatile synthesis of new cytotoxic agents structurally related to hemiasterlins**

pp 3431–3435

Daniele Simoni, Ray M. Lee, David E. Durrant, Nai-Wen Chi, Riccardo Baruchello, Riccardo Rondanin, Cinzia Rullo, Paolo Marchetti*

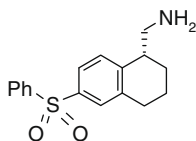


A novel class of hemiasterlin analogues has been depicted, through a highly versatile procedure with control of stereochemistry.

Highly potent, non-basic 5-HT₆ ligands. Site mutagenesis evidence for a second binding mode at 5-HT₆ for antagonism

pp 3436–3440

Ralph N. Harris III*, Russel S. Stabler, David B. Repke, James M. Kress, Keith A. Walker, Renee S. Martin, Julie M. Brothers, Mariola Ilnicka, Simon W. Lee, Tara Mirzadegan



A series of 5-HT₆ ligands derived from (*R*)-1-(amino)methyl-6-(phenyl)sulfonyltetralin was prepared that yielded several neutral, non-basic analogs having sub-nanomolar affinity. Ligand structure–activity relationships, receptor point mutation studies, and molecular modeling of these novel ligands all combined to reveal a new, alternative binding mode to 5-HT₆ for antagonism.

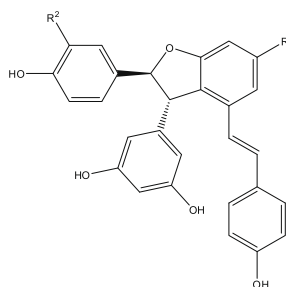


New stilbene dimers against amyloid fibril formation

pp 3441–3443

Céline Rivière, Yorgos Papastamoulis, Pierre-Yves Fortin, Nicolas Delchier, Soahary Andriamanarivo, Pierre Waffo-Teguo, Gilbert D. W. F. Kapche, H. Amira-Guebalia, Jean-Claude Delaunay, Jean-Michel Mérillon, Tristan Richard*, Jean-Pierre Monti*

Two new stilbene dimers could be efficient fibril inhibitors in Alzheimer's disease: scirpusin A and ϵ -viniferin glucoside.



	R ¹	R ²
scirpusin A	OH	OH
ϵ -viniferin glucoside	OGlc	H

*Corresponding author

Supplementary data available via ScienceDirect

COVER

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

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