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Contents

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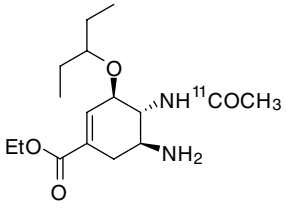
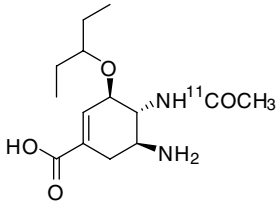
Radiosyntheses of two positron emission tomography probes: [^{11}C]Oseltamivir and its active metabolite [^{11}C]Ro 64-0802 pp 1260–1263

Fujiko Konno, Takuya Arai, Ming-Rong Zhang,* Akiko Hatori, Kazuhiko Yanamoto, Masanao Ogawa, Gukuto Ito, Chika Odawara, Tomoteru Yamasaki, Koichi Kato and Kazutoshi Suzuki

Radiosyntheses of [^{11}C]oseltamivir and its active metabolite [^{11}C]Ro 64-0802 as two positron emission tomography probes and their radioactivity concentrations in the mouse brains are reported for the first time.



[^{11}C]osertamivir

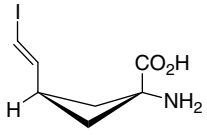


[^{11}C]Ro 64-0802

Synthesis and evaluation of [^{123}I] labeled iodovinyl amino acids *syn*-, *anti*-1-amino-3-[2-iodoethenyl]-cyclobutane-1-carboxylic acid, and 1-amino-3-iodomethylene-cyclobutane-1-carboxylic acid as potential SPECT brain tumor imaging agents pp 1264–1268

Weiping Yu, Larry Williams, Eugene Malveaux, Vernon M. Camp, Jeffrey J. Olson and Mark M. Goodman*

Three [^{123}I] labeled iodovinyl amino acids were synthesized and evaluated in vitro for rat 9L leucine amino acid transporters. Radiolabeling and biodistribution studies in 9L rat glioblastoma model were performed. Compound [^{123}I]**17** showed the highest tumor to brain ratios.

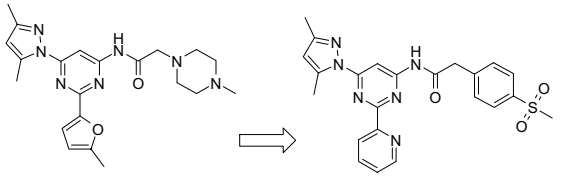


[^{123}I]**17**

2,6-Diaryl-4-phenacylaminopyrimidines as potent and selective adenosine A_{2A} antagonists with reduced hERG liability pp 1269–1273

Manisha Moorjani,* Xiaohu Zhang, Yongsheng Chen, Emily Lin, Jaimie K. Rueter, Raymond S. Gross, Marion C. Lanier, John E. Tellew, John P. Williams, Sandra M. Lechner, Siobhan Malany, Mark Santos, Paddi Ekhlassi, Julio C. Castro-Palomino, María I. Crespo, Maria Prat, Silvia Gual, José-Luis Díaz, John Saunders and Deborah H. Slee

Pyrimidine-based adenosine A_{2A} antagonists were explored to attenuate hERG while improving A_1 selectivity. Replacement of the basic amine side chain led to potent and selective A_{2A} antagonists, with reduced hERG liability.



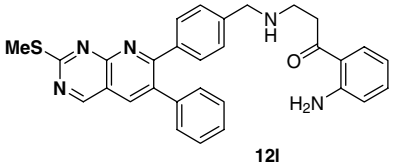
2

Ki (nM) hA_{2A} 12
hA_1/hA_{2A} 71
hERG IC_{50} (nM) 950

33

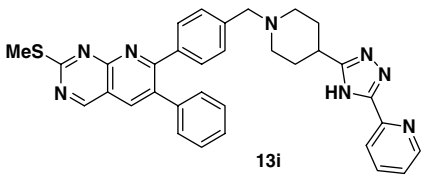
Ki (nM) hA_{2A} 1
hA_1/hA_{2A} 148
hERG IC_{50} (nM) > 4000

Development of Pyridopyrimidines as Potent Akt1/2 Inhibitors **pp 1274–1279**
Zhicai Wu,* John C. Hartnett, Lou Anne Neilson, Ronald G. Robinson, Sheng Fu, Stanley F. Barnett, Deborah Defeo-Jones, Raymond E. Jones, Astrid M. Kral, Hans E. Huber, George D. Hartman and Mark T. Bilodeau



12l

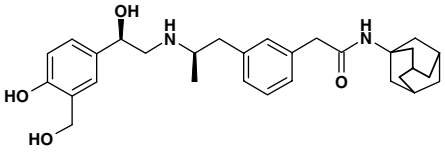
Akt1 IC_{50} = 15 nM, Cell IC_{50} = 78 nM
Akt2 IC_{50} = 90 nM, Cell IC_{50} = 388 nM



13i

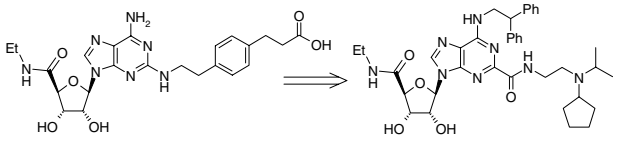
Akt1 IC_{50} = 3.8 nM, Cell IC_{50} = 9.3 nM
Akt2 IC_{50} = 26 nM, Cell IC_{50} = 589 nM

The discovery of adamantyl-derived, inhaled, long acting β_2-adrenoreceptor agonists **pp 1280–1283**
Alan D. Brown, Mark E. Bunnage, Paul A. Glossop, Kim James, Rhys Jones, Charlotte A. L. Lane, Russell A. Lewthwaite, Simon Mantell, Christelle Perros-Huguet, David A. Price,* Mike Trevethick and Rob Webster



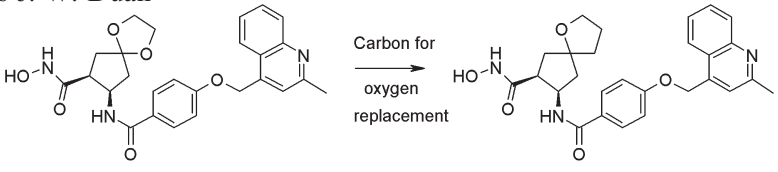
The design and profile of a series of adamantyl-containing long acting β_2-adrenoreceptor agonists are described. An optimal pharmacokinetic profile of low oral bioavailability was combined with a strong pharmacology profile when assessed using a guinea pig trachea tissue model. A focus was then placed on developing a robust synthetic route to ensure rapid delivery of material for clinical trials.

Inhaled adenosine A_{2A} receptor agonists for the treatment of chronic obstructive pulmonary disease **pp 1284–1287**
Simon J. Mantell,* Peter T. Stephenson, Sandra M. Monaghan, Graham N. Maw, Michael A. Trevethick, Michael Yeadon, Ruth F. Keir, Don K. Walker, Rhys M. Jones, Matthew D. Selby, David V. Batchelor, Stuart Rozze, Helene Chavaroche, Tim J. Hobson, Peter G. Dodd, Arnaud Lemaitre, Karen N. Wright and Emilio F. Stuart



The pharmacological and pharmacokinetic SAR of a series of inhaled A_{2A} agonists for the treatment of chronic obstructive pulmonary disease is described.

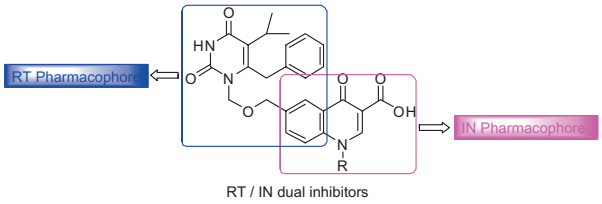
α,β-Cyclic-β-benzamido hydroxamic acids: Novel oxaspiro[4.4]nonane templates for the discovery of potent, selective, orally bioavailable inhibitors of tumor necrosis factor-α converting enzyme (TACE) **pp 1288–1292**
Gregory R. Ott,* Naoyuki Asakawa, Rui-Qin Liu, Maryanne B. Covington, Mingxin Qian, Krishna Vaddi, Robert C. Newton, James M. Trzaskos, David D. Christ, Laurine Galya, Thomas Scholz, Will Marshall and James J.-W. Duan



1 Spiroether-β-benzamido Inhibitors

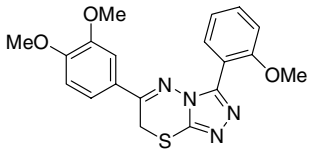
Selective inhibitors of TNF-α Converting Enzyme (TACE) based on novel oxaspiro[4.4]nonane β-benzamido hydroxamic scaffolds acids have been synthesized and evaluated.

Synthesis of pyrimidine and quinolone conjugates as a scaffold for dual inhibitors of HIV reverse transcriptase and integrase pp 1293–1296
Zhengqiang Wang* and Robert Vince*



A series of conjugates combining a pyrimidine and a quinolone moiety were designed and synthesized. These compounds are active against RT and IN and therefore provide a useful scaffold for identifying inhibitors with balanced dual activities.

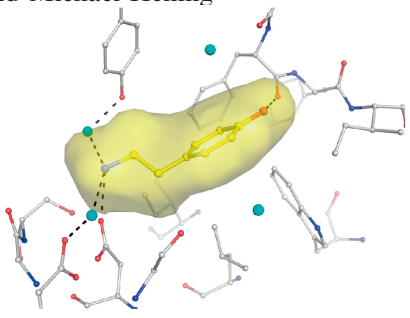
Identification of a potent new chemotype for the selective inhibition of PDE4 pp 1297–1303
Amanda P. Skoumbourdis, Ruili Huang, Noel Southall, William Leister, Vicky Guo, Ming-Hsuang Cho, James Inglese, Marshall Nirenberg, Christopher P. Austin, Menghang Xia and Craig J. Thomas*



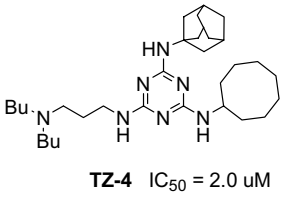
PDE isoform	IC_{50} (μM)
PDE4A	0.024
PDE4B	0.54
PDE4D	0.018

Tyramine fragment binding to BACE-1 pp 1304–1307
Andreas Kuglstatter, Martin Stahl, Jens-Uwe Peters, Walter Huber, Martine Stihle, Daniel Schlatter, Jörg Benz, Armin Ruf, Doris Roth, Thilo Enderle and Michael Hennig*

Tyramine and derivatives thereof bind to the active site of the Alzheimer's disease drug target BACE-1.

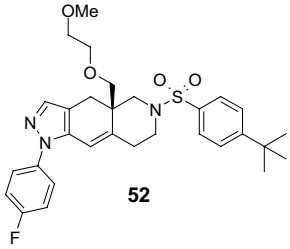


Synthesis and biological evaluation of novel 1,3,5-triazine derivatives as antimicrobial agents pp 1308–1311
Chunhui Zhou, Jaeki Min, Zhigang Liu, Anne Young, Heather Deshazer, Tian Gao, Young-Tae Chang and Neville R. Kallenbach*



1*H*-Pyrazolo[3,4-*g*]hexahydro-isoquinolines as selective glucocorticoid receptor antagonists with high functional activity **pp 1312–1317**
Robin D. Clark,* Nicholas C. Ray, Karen Williams, Paul Blaney, Stuart Ward, Peter H. Crackett, Christopher Hurley, Hazel J. Dyke, David E. Clark, Peter Lockey, Rene Devos, Melanie Wong, Soraya S. Porres, Colin P. Bright, Robert E. Jenkins and Joseph Belanoff

Fusion of the 4-fluorophenylpyrazole group onto the azadecalin system afforded high affinity glucocorticoid receptor (GR) antagonists. The bridgehead position was tolerant to substitution and larger groups afforded optimal GR antagonist functional activity, e.g., methoxyethyl ether **52** had a hGR binding K_i of 0.7 nM and a hGR functional antagonist K_i of 0.6 nM in a reporter gene assay.



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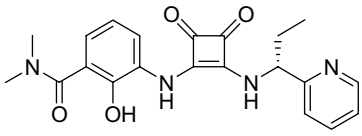
Synthesis and structure–activity relationships of heteroaryl substituted-3,4-diamino-3-cyclobut-3-ene-1,2-dione CXCR2/CXCR1 receptor antagonists **pp 1318–1322**
Younong Yu,* Michael P. Dwyer,* Jianping Chao, Cynthia Aki, Jianhua Chao, Biju Purakkattle, Diane Rindgen, Richard Bond, Rosemary Mayer-Ezel, James Jakway, Hongchen Qiu, R. William Hipkin, James Fossetta, Waldemar Gonsiorek, Hong Bian, Xuedong Fan, Carol Terminelli, Jay Fine, Daniel Lundell, J. Robert Merritt, Zhenmin He, Gaifa Lai, Minglang Wu and Arthur Taveras

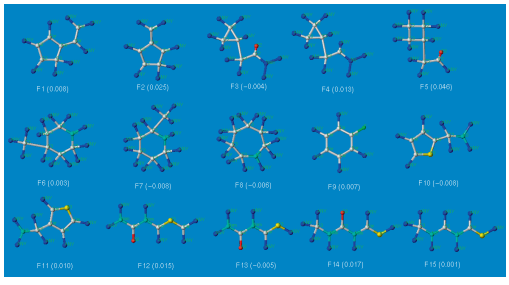
The preparation and biological evaluation of a series of heteroaryl substituted-3,4-diamino-3-cyclobut-3-ene-1,2-dione CXCR2/CXCR1 receptor antagonists (such as **49**) is reported.



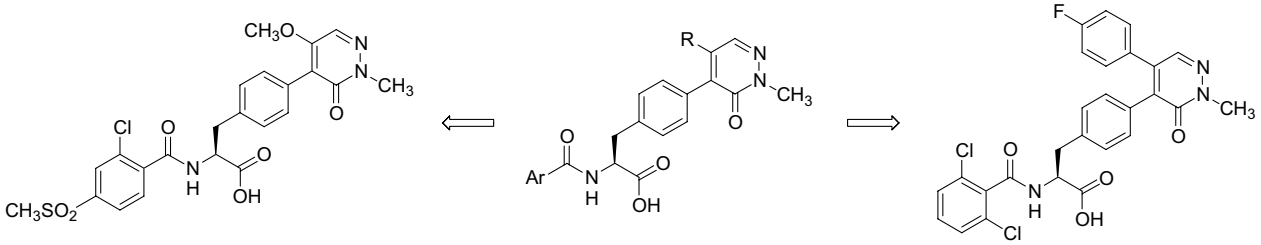
49 CXCR2 IC_{50} = 3.3 nM
CXCR1 IC_{50} = 148 nM

QSAR studies on CCR2 antagonists with chiral sensitive hologram descriptors **pp 1323–1330**
Pramod C. Nair, K. Srikanth and M. Elizabeth Sobhia*

The manuscript reports holographic QSAR studies on CCR2 antagonists with the importance of chirality parameter in model building. The significance of the generated fragments with its relative contributions provides an insight to distinguish S isomer from R counterpart. The fragment information provides useful clues for the design of novel CCR2 antagonists.

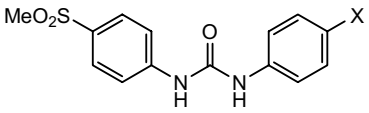


Synthesis and SAR of pyridazinone-substituted phenylalanine amide α_4 integrin antagonists **pp 1331–1335**
Yong Gong,* J. Kent Barbay, Edward S. Kimball, Rosemary J. Santulli, M. Carolyn Fisher, Alexey B. Dyatkin, Tamara A. Miskowski, Pamela J. Hornby and Wei He



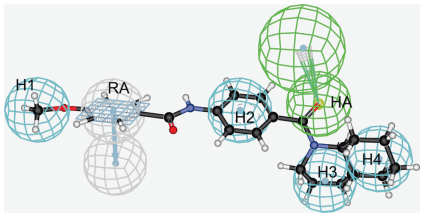
Structure–activity relationships (SAR) within a series of pyridazinone-functionalized phenylalanine amide α_4 integrin antagonists are described.

Design and synthesis of 1,3-diarylurea derivatives as selective cyclooxygenase (COX-2) inhibitors **pp 1336–1339**
Afshin Zarghi,* Samaneh Kakhgi, Atefeh Hadipoor, Bahram Daraee, Orkideh G. Dadrass and Mehdi Hedayati



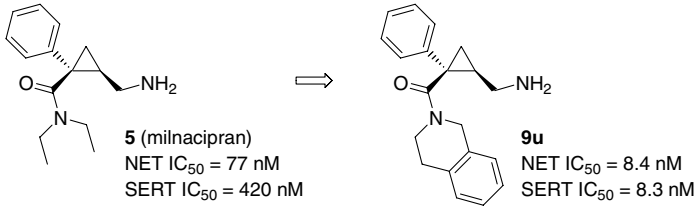
The design, synthesis, and evaluation of a series of 1,3-diarylurea, possessing a methylsulfonyl pharmacophore, as potent and selective COX-2 inhibitors, are described.

Discovery of novel inhibitors of 11β-hydroxysteroid dehydrogenase type 1 by docking and pharmacophore modeling **pp 1340–1345**
Huaiyu Yang, Wei Dou, Jing Lou, Ying Leng* and Jianhua Shen*



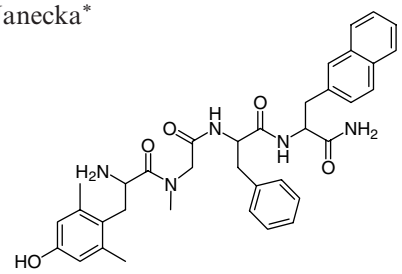
Docking and pharmacophore Modeling were used to discover novel inhibitors of 11β-HSD1. Several compounds with large structural diversity and good potency were found. New scaffolds are reported.

Studies on the SAR and pharmacophore of milnacipran derivatives as monoamine transporter inhibitors **pp 1346–1349**
Chen Chen,* Brian Dyck, Beth A. Fleck, Alan C. Foster, Jonathan Grey, Florence Jovic, Michael Mesleh, Kasey Phan, Junko Tamiya, Troy Vickers and Mingzhu Zhang



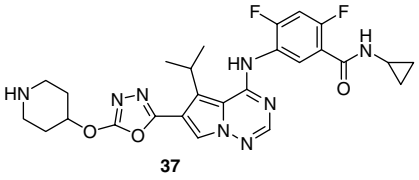
Novel highly potent μ-opioid receptor antagonist based on endomorphin-2 structure **pp 1350–1353**
Jakub Fichna, Jean-Claude do-Rego, Tomasz Janecki, Renata Staniszewska, Jeroen Poels, Jozef Vanden Broeck, Jean Costentin, Peter W. Schiller and Anna Janecka*

A novel extremely selective μ-opioid receptor antagonist of a peptide structure is reported.



[Dmt[1], Sar[2], D-2-Nal[4]]endomorphin-2

Synthesis, SAR, and Evaluation of 4-[2,4-Difluoro-5-(cyclopropylcarbamoyl)phenylamino]pyrrolo[2,1-*f*][1,2,4]triazine-based VEGFR-2 kinase inhibitors **pp 1354–1358**
Zhen-wei Cai,* Donna Wei, Robert M. Borzilleri, Ligang Qian, Amrita Kamath, Steven Mortillo, Barri Wautlet, Benjamin J. Henley, Robert Jeyaseelan, Sr., John Tokarski, John T. Hunt, Rajeev S. Bhide, Joseph Fargnoli and Louis J. Lombardo

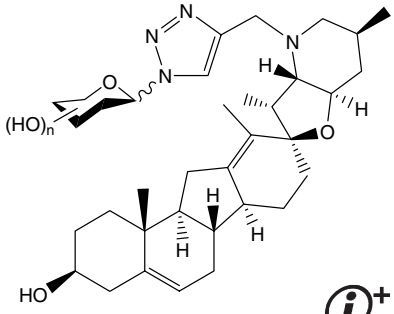


37

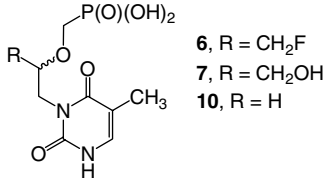
A new sub-family of pyrrolotriazine analogs was identified as the potent VEGFR-2 kinase inhibitors. Antitumor efficacy was observed with compound **37** against L2987 human lung carcinoma xenografts in athymic mice.

Synthesis and anticancer activity studies of cyclopamine derivatives **pp 1359–1363**
Jianjun Zhang, Massoud Garrossian, Dale Gardner, Arash Garrossian, Young-Tae Chang, Yun Kyung Kim and Cheng-Wei Tom Chang*

A diversity-oriented synthesis has been developed for facile construction of a library of carbohydrate–cyclopamine conjugates. The synthetic protocol is suitable for generating cyclopamine derivatives with various structural motifs for exploring the desired activity. From this initial library, we have observed one derivative that exhibits improved activity against lung cancer cell as compared to cyclopamine.



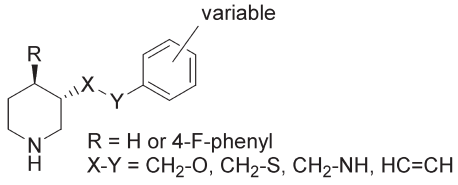
Syntheses of N^3-substituted thymine acyclic nucleoside phosphonates and a comparison of their inhibitory effect towards thymidine phosphorylase **pp 1364–1367**
Karel Pomeisl,* Antonín Holý, Ivan Votruba and Radek Pohl



6, R = CH_2F
7, R = CH_2OH
10, R = H

The synthesis and a comparison of inhibitory activity toward thymidine phosphorylase for N^3-substituted thymine acyclic nucleoside phosphonate analogues **6**, **7**, and **10** of multisubstrate inhibitors is reported.

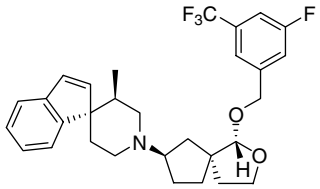
Synthesis and evaluation of PSSRI-based inhibitors of *Staphylococcus aureus* multidrug efflux pumps **pp 1368–1373**
Nadezhda German, Glenn W. Kaatz and Robert J. Kerns*



R = H or 4-F-phenyl
X-Y = CH_2-O, CH_2-S, CH_2-NH, HC=CH

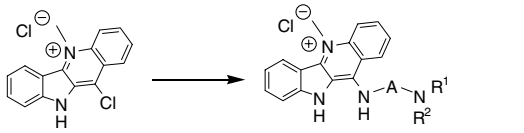
Conformational studies of 3-amino-1-alkyl-cyclopentane carboxamide CCR2 antagonists leading to new spirocyclic antagonists **pp 1374–1377**
Alexander Pasternak,* Stephen D. Goble, George A. Doss, Nancy N. Tsou, Gabor Butora, Pasquale P. Vicario, Julia Marie Ayala, Mary Struthers, Julie A. DeMartino, Sander G. Mills and Lihu Yang

Evaluation of CCR2 binding affinities of conformationally constrained CCR2 antagonist analogs gave insight into the optimal relative positions of the piperidine and benzylamide moieties while simultaneously leading to the discovery of a new, potent lead type based upon a spirocyclic acetal scaffold.



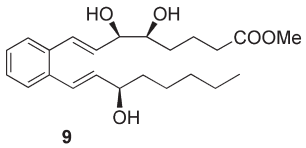
8b

Cryptolepine analogues containing basic aminoalkyl side-chains at C-11: Synthesis, antiplasmodial activity, and cytotoxicity **pp 1378–1381**
João Lavrado, Alexandra Paulo, Jiri Gut, Philip J. Rosenthal and Rui Moreira*



Cryptolepine derivatives containing a basic short chain at position C-11 present IC_{50} values against the chloroquine-resistant *Plasmodium falciparum* W2 strain ranging from 22 to 184 nM.

Design and synthesis of benzo-lipoxin A_4 analogs with enhanced stability and potent anti-inflammatory properties **pp 1382–1387**
Nicos A. Petasis,* Raquel Keledjian, Yee-Ping Sun, Kalyan C. Nagulapalli, Eric Tjonahen, Rong Yang and Charles N. Serhan

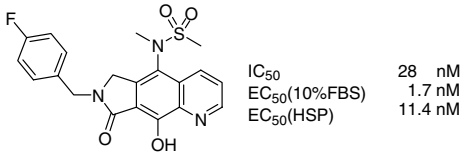


9

o-[9,12]-Benzo-15-epi LXA_4 methyl ester

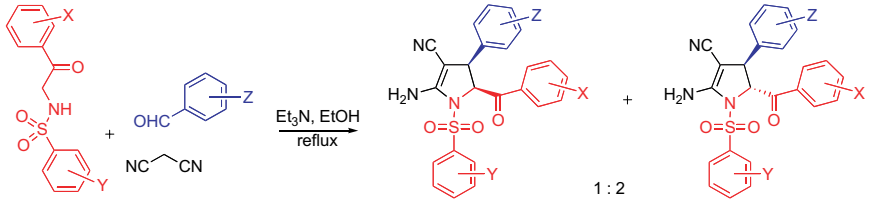
New types of benzo-lipoxin A_4 analogs, such as **9**, were synthesized and shown to have potent anti-inflammatory properties by suppressing neutrophil infiltration in vivo.

Tricyclic HIV integrase inhibitors: Potent and orally bioavailable C5-aza analogs **pp 1388–1391**
Haolun Jin,* Matthew Wright, Richard Pastor, Michael Mish, Sammy Metobo, Salman Jabri, Rachael Lansdown, Ruby Cai, Peter Pyun, Manuel Tsiang, Xiaowu Chen and Choung U. Kim

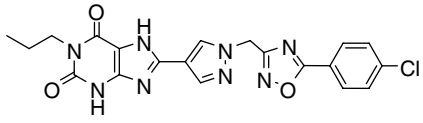


The design and preparation of highly potent tricyclic HIV integrase inhibitors are reported. The lead compound has shown good oral bioavailability in both rat and dog.

Novel three-component synthesis and antiproliferative properties of diversely functionalized pyrrolines **pp 1392–1396**
Igor V. Magedov,* Giovanni Luchetti, Nikolai M. Evdokimov, Madhuri Manpadi, Wim F. A. Steelant, Severine Van slambrouck, Paul Tongwa, Mikhail Yu. Antipin and Alexander Kornienko*

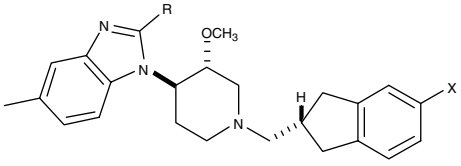


Selective, high affinity A_{2B} adenosine receptor antagonists: N-1 monosubstituted 8-(pyrazol-4-yl)xanthines **pp 1397–1401**
Rao V. Kalla,* Elfatih Elzein, Thao Perry, Xiaofen Li, Art Gimbel, Ming Yang, Dewan Zeng and Jeff Zablocki



We describe the synthesis of a series of N-1 monosubstituted 8-pyrazolyl xanthines, as high affinity and selective adenosine A_{2B} receptor antagonists. [**CVT-6694**; A_{2B} AdoR K_i = 7 nM, selectivity A_1 > 850: A_{2A} > 700: A_3 > 1280].

Potent, selective MCH-1 receptor antagonists **pp 1402–1406**
Shawn D. Erickson,* Bruce Banner, Steven Berthel, Karin Conde-Knape, Fiorenza Falcioni, Irina Hakimi, Bernard Hennessy, Robert F. Kester, Kyungjin Kim, Chun Ma, Warren McComas, Francis Mennona, Steven Mischke, Lucy Orzechowski, Yimin Qian, Hamid Salari, John Tengi, Kshitij Thakkar, Rebecca Taub, Jefferson W. Tilley and Hong Wang

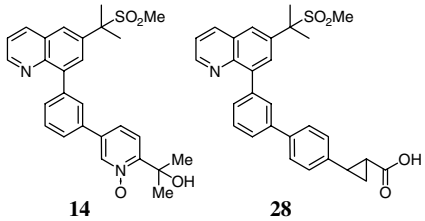


X = -Br, -CN, -H
R = $-CH_3$, $C(CH_3)_2OH$

The design and synthesis of potent and selective indanylmethylpiperidine-based MCHR1 antagonists is reported.

Design, synthesis, and biological evaluation of 8-biarylquinolines: A novel class of PDE4 inhibitors **pp 1407–1412**
Michel Gallant,* Nathalie Chauret, David Claveau, Stephen Day, Denis Deschênes, Daniel Dubé, Zheng Huang, Patrick Lacombe, France Laliberté, Jean-François Lévesque, Susana Liu, Dwight Macdonald, Joseph Mancini, Paul Masson, Anthony Mastracchio, Donald Nicholson, Deborah A. Nicoll-Griffith, Hélène Perrier, Myriam Salem, Angela Styhler, Robert N. Young and Yves Girard

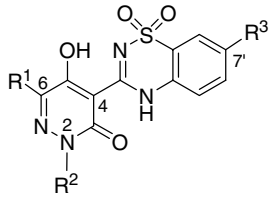
The structure–activity relationship of a novel series of 8-biarylquinolines acting as type 4 phosphodiesterase (PDE4) inhibitors is described herein. Prototypical compounds from this series are potent (IC_{50} < 10 nM) but displayed little or no isozyme specificity. Optimized inhibitors were evaluated in vivo for efficacy in an ovalbumin-induced bronchoconstriction model in conscious guinea pigs. This work has led to the identification of compounds **14** and **28** which display excellent in vitro and in vivo profiles, including a good therapeutic window of efficacy over emesis.



14 **28**

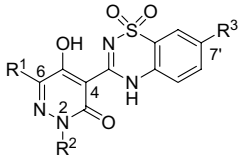
Novel HCV NS5B polymerase inhibitors derived from 4-(1′,1′-dioxo-1′,4′-dihydro-1′λ^6-benzo[1′,2′,4′]thiadiazin-3′-yl)-5-hydroxy-2*H*-pyridazin-3-ones. Part 1: Exploration of 7′-substitution of benzothiadiazine pp 1413–1418

Yuefen Zhou,* Stephen E. Webber, Douglas E. Murphy, Lian-Sheng Li, Peter S. Dragovich, Chinh V. Tran, Zhongxiang Sun, Frank Ruebsam, Amit M. Shah, Mei Tsan, Richard E. Showalter, Rupal Patel, Bin Li, Qiang Zhao, Qing Han, Thomas Hermann, Charles R. Kissinger, Laurie LeBrun, Maria V. Sergeeva and Leo Kirkovsky



Novel HCV NS5B polymerase inhibitors derived from 4-(1′,1′-dioxo-1′,4′-dihydro-1′λ^6-benzo[1′,2′,4′]thiadiazin-3′-yl)-5-hydroxy-2*H*-pyridazin-3-ones. Part 2: Variation of the 2- and 6-pyridazinone substituents pp 1419–1424

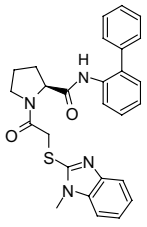
Yuefen Zhou,* Lian-Sheng Li, Peter S. Dragovich, Douglas E. Murphy, Chinh V. Tran, Frank Ruebsam, Stephen E. Webber, Amit M. Shah, Mei Tsan, April Averill, Richard E. Showalter, Rupal Patel, Qing Han, Qiang Zhao, Thomas Hermann, Charles R. Kissinger, Laurie LeBrun and Maria V. Sergeeva



Proline bis-amides as potent dual orexin receptor antagonists pp 1425–1430

Jeffrey M. Bergman,* Anthony J. Roecker, Swati P. Mercer, Rodney A. Bednar, Duane R. Reiss, Richard W. Ransom, C. Meacham Harrell, Douglas J. Pettibone, Wei Lemaire, Kathy L. Murphy, Chunze Li, Thomayant Prueksaritanont, Christopher J. Winrow, John J. Renger, Kenneth S. Koblan, George D. Hartman and Paul J. Coleman

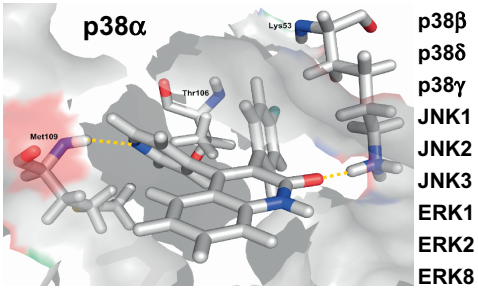
A series of potent dual orexin antagonists was prepared based on a proline bis-amide core that demonstrate in vivo central activity in a pharmacodyamic model of orexin activity.



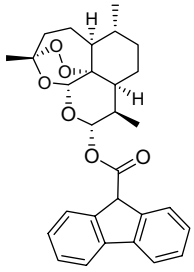
hOX2R Ki (nM)[a] = 0.2
hOX1R Ki (nM)[a] = 3

Implications for selectivity of 3,4-diarylquinolinones as p38αMAP kinase inhibitors pp 1431–1435

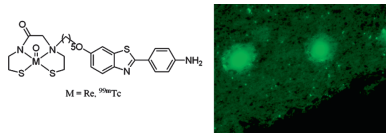
Christian Peifer,* Robert Urich, Verena Schattel, Mohammed Abadleh, Marc Röttig, Oliver Kohlbacher and Stefan Laufer



Orally active esters of dihydroartemisinin: Synthesis and antimalarial activity against multidrug-resistant *Plasmodium yoelii* in mice pp 1436–1441
Chandan Singh,* Sandeep Chaudhary and Sunil K. Puri

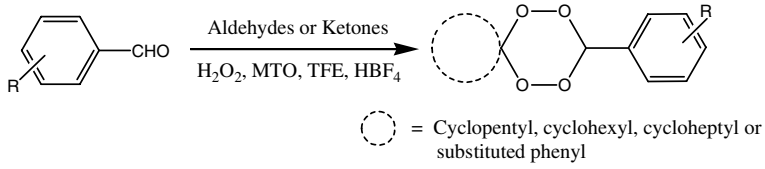


Synthesis and biological evaluation of ^{99m}Tc, Re-monoamine-monoamide conjugated to 2-(4-aminophenyl)benzothiazole as potential probes for β-amyloid plaques in the brain pp 1442–1445
Xiangji Chen, Pingrong Yu, Lianfeng Zhang and Boli Liu*



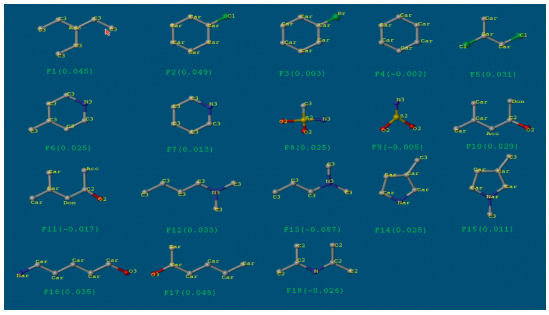
The synthesis and biological evaluation of ^{99m}Tc, Re-MAMA-BTA were reported here.

Synthesis, thermal stability, antimalarial activity of symmetrically and asymmetrically substituted tetraoxanes pp 1446–1449
Himanshu Atheaya, Shabana I. Khan, Ritu Mamgain and Diwan S. Rawat*

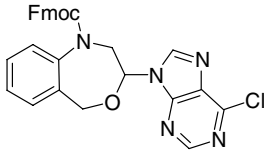


Probing the structural and topological requirements for CCR2 antagonism: Holographic QSAR for indolopiperidine derivatives pp 1450–1456
K. Srikanth, Pramod C. Nair and M. Elizabeth Sobhia*

A holographic QSAR study performed on a set of indolopiperidine derivatives acting as CCR2 antagonists is reported. Analysis of hologram fingerprints throws light on essential structural and topological features of indolopiperidine derivatives for CCR2 antagonism.



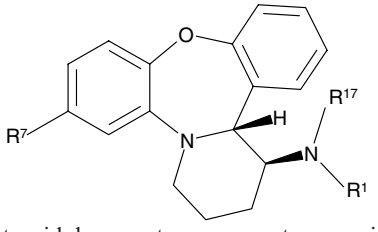
Anticancer activity of (1,2,3,5-tetrahydro-4,1-benzoxazepine-3-yl)-pyrimidines and -purines against the MCF-7 cell line: Preliminary cDNA microarray studies pp 1457–1460
Mónica Díaz-Gavilán, José A. Gómez-Vidal, Fernando Rodríguez-Serrano, Juan A. Marchal, Octavio Caba, Antonia Aránega, Miguel A. Gallo, Antonio Espinosa and Joaquín M. Campos*



28 IC_{50} = 0.67 μM

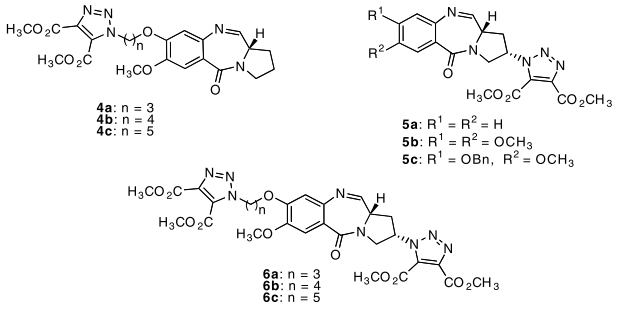
To the best of our knowledge, the *O*,*N*-acetal 28 represents a new kind of compound with a novel structure and a significant activity against the MCF-7 cell line.

SAR study of 2,3,4,14b-tetrahydro-1*H*-dibenzo[*b*,*f*]pyrido[1,2-*d*][1,4]oxazepines as progesterone receptor agonists pp 1461–1467
Paul P. M. A. Dols, Brigitte J. B. Folmer, Hans Hamersma, Cor W. Kuil, Hans Lucas, Lourdes Ollero, Jos B. M. Rewinkel and Pedro H. H. Hermkens*



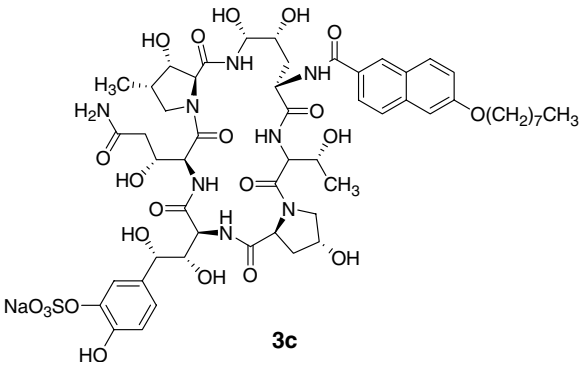
The synthesis and SAR of a new class of non-steroidal progesterone receptor agonists having a tetracyclic dibenzo-oxazepine structure are described.

Synthesis of 1,2,3-triazole-linked pyrrolobenzodiazepine conjugates employing 'click' chemistry: DNA-binding affinity and anticancer activity pp 1468–1473
Ahmed Kamal,* N. Shankaraiah, V. Devaiah, K. Laxma Reddy, Aarti Juvekar, Subrata Sen, Nisha Kurian and Surekha Zingde

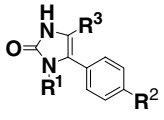


Novel echinocandin antifungals. Part 1: Novel side-chain analogs of the natural product FR901379 pp 1474–1477
Masaki Tomishima,* Hidenori Ohki, Akira Yamada, Katsuyuki Maki and Fumiaki Ikeda

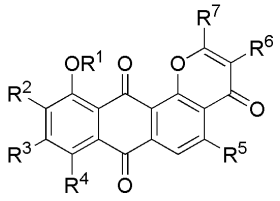
A series of novel acylated analogs of the novel water-soluble echinocandin FR901379 have been prepared. Compound **3c** shows both potent antifungal activity and weak hemolytic activity.



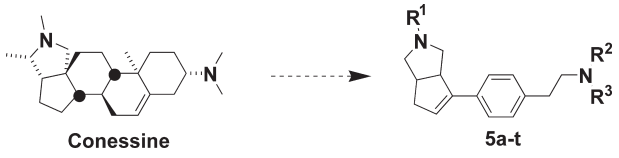
5-Aryl-imidazolin-2-ones as a scaffold for potent antioxidant and memory-improving activity **pp 1478–1483**
Kazutoshi Watanabe,* Yasuhiro Morinaka, Yoshio Hayashi, Masaki Shinoda, Hiroyoshi Nishi, Nobuko Fukushima, Toshiaki Watanabe, Akira Ishibashi, Satoshi Yuki and Masahiko Tanaka



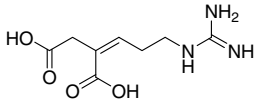
Synthesis and cytotoxic activity of a new series of topoisomerase I inhibitors **pp 1484–1489**
Sabrina Dallavalle,* Sonia Gattinoni, Stefania Mazzini, Leonardo Scaglioni, Lucio Merlini, Stella Tinelli, Giovanni L. Beretta and Franco Zunino



A new family of H_3 receptor antagonists based on the natural product Conessine **pp 1490–1494**
Vincent J. Santora,* Jonathan A. Covel, Rena Hayashi, Brian J. Hofilena, Jason B. Ibarra, Michelle D. Pulley, Michael I. Weinhouse, Dipanjan Sengupta, Jonathan J. Duffield, Graeme Semple, Robert R. Webb, Carleton Sage, Albert Ren, Guilherme Pereira, Jens Knudsen, Jeffrey E. Edwards, Marissa Suarez, John Frazer, William Thomsen, Erin Hauser, Kevin Whelan and Andrew J. Grottick



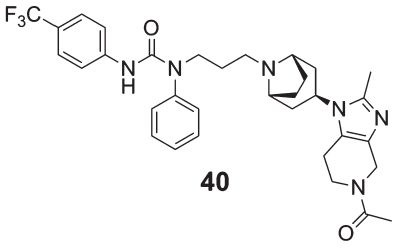
Lysianadioic acid, a carboxypeptidase B inhibitor from *Lysiana subfalcata* **pp 1495–1497**
Malcolm S. Buchanan, Anthony R. Carroll, Annette Edser, Melissa Sykes, Gregory A. Fechner, Paul I. Forster, Gordon P. Guymer and Ronald J. Quinn*


Lysianadioic acid

Lysianadioic acid, a small molecule inhibitor of CPB, was isolated from *Lysiana subfalcata*. It is a new arginine analogue containing an unusual dicarboxylic acid moiety and is the first known example of a small molecule CPB inhibitor isolated from plant origin.

Anti-HIV-1 entry optimization of novel imidazopiperidine-tropane CCR5 antagonists **pp 1498–1501**
Justin Ernst,* Russell Dahl, Christopher Lum, Lubomir Sebo, Jan Urban, Stephen G. Miller and Jan Lundström

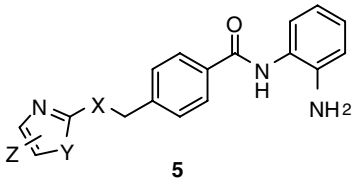
A novel series of imidazopiperidine-tropane CCR5 antagonists is described. The series was optimized for anti-HIV-1 potency using a set of phenotypic viral entry assays. This strategy resulted in the identification of several very potent (IC_{50} < 10 nM) inhibitors of HIV-1 entry. One compound (**40**) was further profiled and was found to have attractive selectivity, pharmacokinetic, and antiviral properties.



40

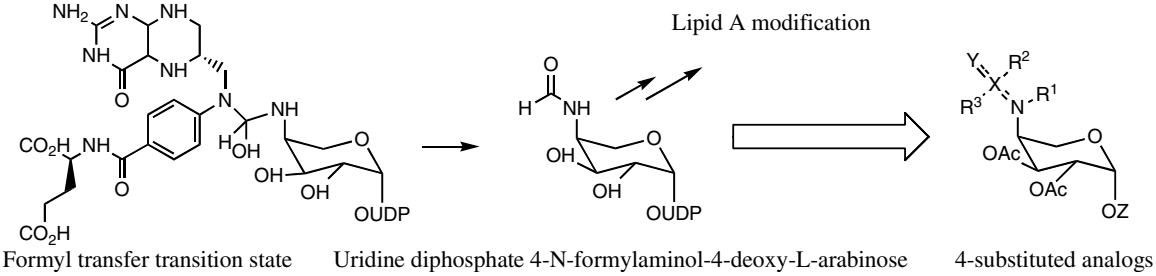
4-(Heteroarylaminomethyl)-*N*-(2-aminophenyl)-benzamides and their analogs as a novel class of histone deacetylase inhibitors **pp 1502–1506**
Sylvie Fréchette,* Silvana Leit, Soon Hyung Woo, Guillaume Lapointe, Guillaume Jeannotte, Oscar Moradei, Isabelle Paquin, Giliane Bouchain, Stéphane Raeppel, Frédéric Gaudette, Nancy Zhou, Arkadii Vaisburg, Marielle Fournel, Pu Theresa Yan, Marie-Claude Trachy-Bourget, Ann Kalita, Marie-France Robert, Aihua Lu, Jubrail Rahil, A. Robert MacLeod, Jeffrey M. Besterman, Zuomei Li and Daniel Delorme

The synthesis and biological evaluation as histone deacetylase (HDAC) inhibitors of a variety of 4-(heteroarylaminomethyl)-*N*-(2-aminophenyl)-benzamides of general structure **5** is described.



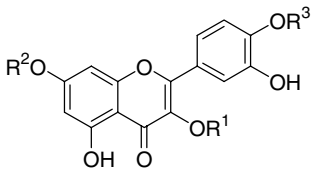
5

Synthesis of and evaluation of lipid A modification by 4-substituted 4-deoxy arabinose analogs as potential inhibitors of bacterial polymyxin resistance **pp 1507–1510**
T. Kline,* M. S. Trent, C. M. Stead, M. S. Lee, M. C. Sousa, H. B. Felise, H. V. Nguyen and S. I. Miller



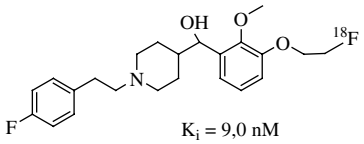
Formyl transfer transition state Uridine diphosphate 4-N-formylaminol-4-deoxy-L-arabinose 4-substituted analogs

In vitro anti-inflammatory activity of 3-*O*-methyl-flavones isolated from *Siegesbeckia glabrescens* **pp 1511–1514**
Jae Yeon Kim, Hyo Jin Lim and Jae-Ha Ryu*



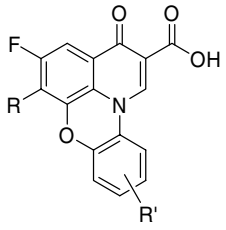
Four quercetin derivatives from *Siegesbeckia glabrescens* inhibited the production of nitric oxide and the expression of iNOS in LPS-activated microglia.

Total synthesis and evaluation of [^{18}F]MHMZ **pp 1515–1519**
Matthias M. Herth,* Fabian Debus, Markus Piel, Mikael Palner, Gitte M. Knudsen, Hartmut Lüddens and Frank Rösch

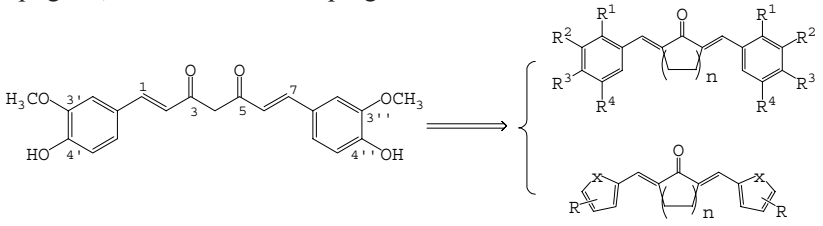


The synthesis and evaluation of [^{18}F]MHMZ, a potential 5-HT_{2A} antagonist (K_i = 9.0 nM), is reported.

New insight for fluoroquinophenoxazine derivatives as possibly new potent topoisomerase I inhibitor **pp 1520–1524**
Da-Hye Kang, Jung-Sook Kim, Mi-Ja Jung, Eung-Seok Lee, Yurngdong Jahng, Youngjoo Kwon* and Younghwa Na*

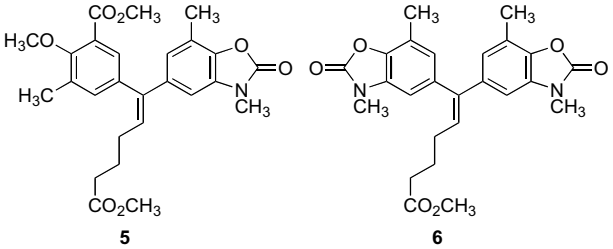


Synthesis and anti-inflammatory activities of mono-carbonyl analogues of curcumin **pp 1525–1529**
Guang Liang, Xiaokun Li,* Li Chen, Shulin Yang, Xudong Wu, Elaine Studer, Emily Gurley, Phillip B. Hylemon, Faqing Ye, Yueru Li and Huiping Zhou*



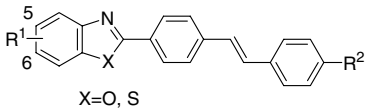
A series of mono-carbonyl curcumin analogues with more stable chemical structures were synthesized and several compounds showed an enhanced ability to inhibit lipopolysaccharide (LPS)-induced TNF-α and IL-6 synthesis in macrophages.

Investigation of the alkenyldiarylmethane non-nucleoside reverse transcriptase inhibitors as potential cAMP phosphodiesterase-4B2 inhibitors **pp 1530–1533**
Matthew D. Cullen, York-Fong Cheung, Miles D. Houslay, Tracy L. Hartman, Karen M. Watson, Robert W. Buckheit, Christophe Pannecouque, Erik De Clercq and Mark Cushman*



Synthesis and evaluation of stilbenylbenzoxazole and stilbenylbenzothiazole derivatives for detecting β-amyloid fibrils **pp 1534–1537**
Ji Hoon Lee, Seong Rim Byeon, Soo Jeong Lim, Seung Jun Oh, Dae Hyuk Moon, Kyung Ho Yoo, Bong Young Chung* and Dong Jin Kim*

Novel series of stilbenylbenzoxazole (**SBO**) and stilbenylbenzothiazole (**SBT**) derivatives were synthesized and evaluated by competitive binding assay against β-amyloid 1–42 (Aβ42) aggregates using [^{125}I]TZDM. All the derivatives displayed higher binding affinities with K_i values in the subnanomolar range (0.10–0.74 nM) than PIB (0.77 nM). In conclusion, the preliminary results suggest that these compounds are implying a possibility as a probe for detection of Aβ fibrils in Alzheimer's disease (AD) patients.



X=O, S
R^1=$O(CH_2)_2F$, $O(CH_2)_3F$
R^2=NH_2, $NHCH_3$, $N(CH_3)_2$

OTHER CONTENTS

Summary of instructions to authors **p I**

*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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