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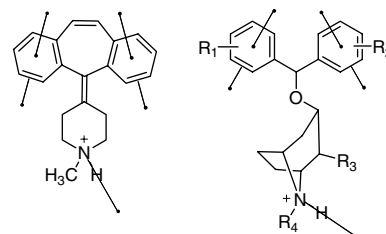
ARTICLES

Comparative structure–activity relationships of benztropine analogues at the dopamine transporter and histamine H₁ receptors

pp 3625–3634

Santosh S. Kulkarni, Theresa A. Kopajtic, Jonathan L. Katz and Amy Hauck Newman*

Many benztropine analogues bind with high affinity to the dopamine transporter (DAT). They also show a wide range ($K_i = 16\text{--}37,600\text{ nM}$) of binding affinities at the histamine H₁ receptor. A structural comparison of activity and selectivity at the DAT and the histamine H₁ receptor was performed in order to identify structural requirements and differences for optimal binding to each site and selectivity for the DAT.

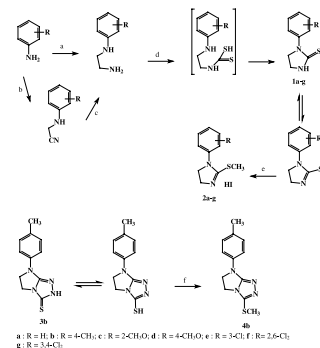


Synthesis of imidazoline and imidazo[2,1-*c*][1,2,4]triazole aryl derivatives containing the methylthio group as possible antibacterial agents

pp 3635–3642

Krzysztof Sztanke,* Kazimierz Pasternak, Anna Sidor-Wójtowicz, Janina Truchlińska and Krzysztof Jówiak

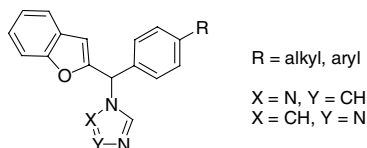
Biologically active imidazoline and imidazo[2,1-*c*][1,2,4]triazole aryl derivatives containing the methylthio group were synthesized and evaluated for their in vitro antimicrobial activity against a panel of Gram-positive and Gram-negative bacteria, moulds and yeast-like fungi including clinical isolates. All tested compounds (**2a–g** and **4b**) showed MIC in the range of 11.0–89.2 μM . Compounds **2a,e** were found to be equipotent to chloramphenicol in vitro, whereas **2a,c,e–g** and **4b** showed superior activity (MIC) to ampicillin.



Synthesis and CYP26A1 inhibitory activity of 1-[benzofuran-2-yl-(4-alkyl/aryl-phenyl)-methyl]-1*H*-triazoles

pp 3643–3653

Stephane Pautus, Sook Wah Yee, Martyn Jayne, Michael P. Coogan and Claire Simons*



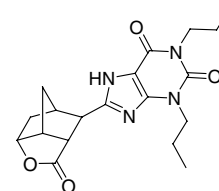
A series of 4-alkyl/aryl-substituted 1-[benzofuran-2-yl-phenylmethyl]-1*H*-[1,2,4] and [1,3,4]triazoles derivatives were prepared and evaluated for CYP26A1 inhibitory activity using a MCF-7 cell based assay. The 4-ethyl and 4-phenyl-1,2,4-triazole derivatives displayed inhibitory activity (IC_{50} 4.5 and 7 μM , respectively) comparable with the CYP26 inhibitor liarozole (IC_{50} 7 μM). Using a CYP26A1 homology model, docking experiments were performed with the inhibitor compounds.

Norbornylactone-substituted xanthines as adenosine A₁ receptor antagonists

pp 3654–3661

William F. Kiesman,* Jin Zhao, Patrick R. Conlon, Russell C. Petter, Xiaowei Jin, Glenn Smits, Frank Lutterodt, Gail W. Sullivan and Joel Linden

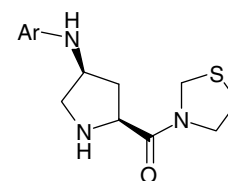
During the search for second-generation adenosine A₁ receptor antagonist alternatives to the clinical candidate 8-(3-oxa-tricyclo[3.2.1.0^{2,4}]oct-6-yl)-1,3-dipropyl-3,7-dihydro-purine-2,6-dione (BG9719), we developed a series of novel xanthines substituted with norbornyl-lactones that possessed high binding affinities for adenosine A₁ receptors and in vivo activity.

**[(S)-γ-(Arylamino)prolyl]thiazolidine compounds as a novel series of potent and stable DPP-IV inhibitors**

pp 3662–3671

Hiroshi Sakashita, Fumihiko Akahoshi,* Hiroshi Kitajima, Reiko Tsutsumiuchi and Yoshiharu Hayashi

[(S)-γ-(Arylamino)prolyl]thiazolidine compounds were synthesized and evaluated as a novel series of potent and stable DPP-IV inhibitors. The 3,4-dicyanophenylamino-substituted compound **12m** showed the most potent inhibitory activity, while the (5-cyano-2-pyridyl)amino-substituted compound **11** exhibited an excellent pharmacokinetic profile.



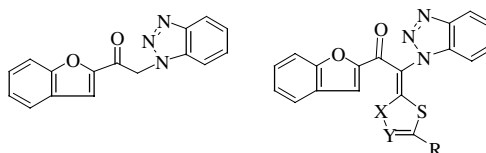
11: Ar = 5-cyano-2-pyridyl

12m: Ar = 3,4-dicyanophenyl

Synthesis, anticonvulsant, and anti-inflammatory evaluation of some new benzotriazole and benzofuran-based heterocycles

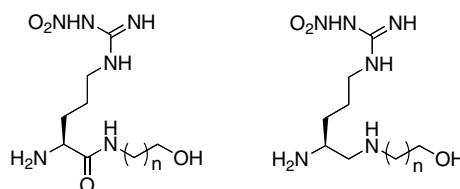
pp 3672–3680

Kamal M. Dawood,* Hassan Abdel-Gawad, Eman A. Rageb, Mohey Ellithey and Hanan A. Mohamed

**Hydroxyl-terminated peptidomimetic inhibitors of neuronal nitric oxide synthase**

pp 3681–3690

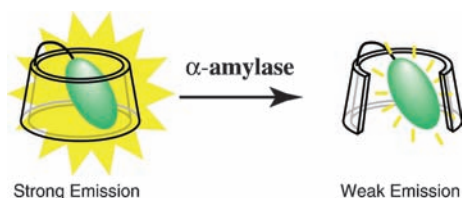
Bessie N. A. Mbadugha, Jiwon Seo, Haitao Ji, Pavel Martásek, Linda J. Roman, Thomas M. Shea, Huiying Li, Thomas L. Poulos and Richard B. Silverman*



Direct assay for α -amylase using fluorophore-modified cyclodextrins

pp 3691–3696

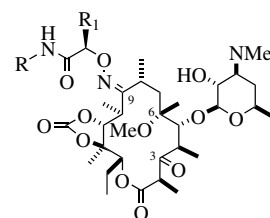
Takuya Murayama, Tetsuya Tanabe, Hiroshi Ikeda* and Akihiko Ueno

**A new type of ketolide bearing an *N*-aryl-alkyl acetamide moiety at the C-9 iminoether: Synthesis and structure–activity relationships (2)**

pp 3697–3711

Takashi Nomura,* Tsutomu Iwaki, Yukitoshi Narukawa, Koichi Uotani, Toshihiko Hori and Hideaki Miwa

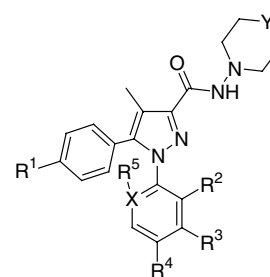
A new type of ketolide bearing an *N*-aryl-alkyl acetamide moiety at the C-9 iminoether and its analogues were prepared, and their antibacterial activities and pharmacokinetic properties were evaluated. We found that the introduction of an (*R*)-alkyl group between the amide and iminoether groups could improve the pharmacokinetic properties while maintaining the activity against erythromycin-resistant *Streptococcus pneumoniae*.

**Synthesis and structure–activity relationships (SARs) of 1,5-diarylpyrazole cannabinoid type-1 (CB₁) receptor ligands for potential use in molecular imaging**

pp 3712–3720

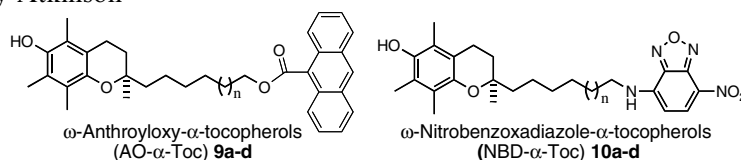
Sean R. Donohue,* Christer Halldin and Victor W. Pike

Synthesis, pharmacology, and calculated lipophilicities of a series of 1,5-diarylpyrazole cannabinoid type-1 (CB₁) receptor ligands as prospective radioligands for in vivo imaging.

**Preparation of fluorescent tocopherols for use in protein binding and localization with the α -tocopherol transfer protein**

pp 3721–3736

Phillip Nava, Matt Cecchini, Sara Chirico, Heather Gordon, Samantha Morley, Danny Manor and Jeffrey Atkinson*

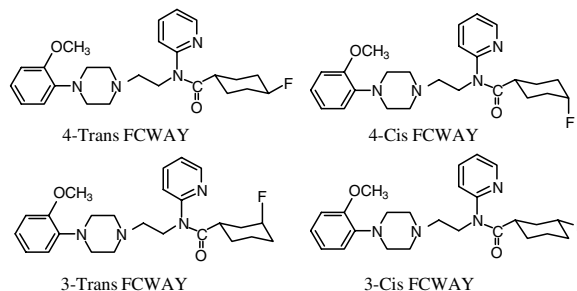


The aim of this work was to prepare and demonstrate the utility of fluorescent analogues of α -tocopherol as probes for use in protein-binding assays, intracellular localization studies, and transfer assays using vesicles and the tocopherol transfer protein, α -TTP. The NBD- α -tocopherols proved to be excellent ligands of recombinant human α -TTP. One AO- α -tocopherol ($n = 4$), while still useful, is limited by its very low solubility in buffers.

Synthesis and in vivo biodistribution of F-18 labeled 3-*cis*-, 3-*trans*-, 4-*cis*-, and 4-*trans*-fluorocyclohexane derivatives of WAY 100635

pp 3737–3748

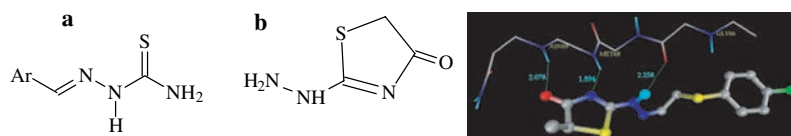
Lixin Lang,* Elaine Jagoda, Ying Ma, Mark B. Sassaman and William C. Eckelman



Synthesis, docking, and in vitro activity of thiosemicarbazones, aminoacyl-thiosemicarbazides and acyl-thiazolidones against *Trypanosoma cruzi*

pp 3749–3757

Ana Cristina Lima Leite,* Renata Souza de Lima, Diogo Rodrigo de M. Moreira, Marcos Veríssimo de O. Cardoso, Ana Carolina Gouveia de Brito, Luciene Maria Farias dos Santos, Marcelo Zaldini Hernandez, Alice Costa Kiperstok, Ricardo Santana de Lima and Milena B. P. Soares

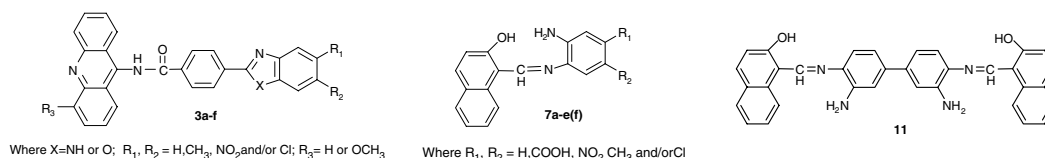


A novel series of thiosemicarbazone and aminoacyl-thiazolidone derivatives were synthesized. Biological evaluation indicates that some of these compounds are able to inhibit the growth of *Trypanosoma cruzi* in concentrations non-cytotoxic to mammalian cells. Docking studies of these compounds for the *T. cruzi* cruzain (TCC) protein showed a significant correlation with experimental data.

Synthesis, anti-inflammatory, analgesic and kinase (CDK-1, CDK-5 and GSK-3) inhibition activity evaluation of benzimidazole/benzoxazole derivatives and some Schiff's bases

pp 3758–3765

Sham M. Sondhi,* Nirupma Singh, Ashok Kumar, Olivier Lozach and Laurent Meijer



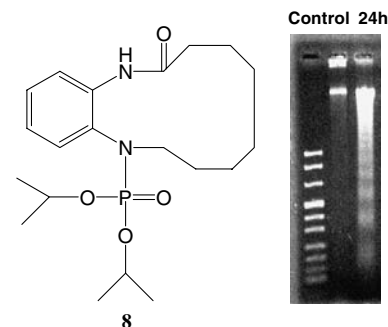
A series of *N*-(acridin-9-yl)-4-(benzo[d]imidazol/oxazol-2-yl)benzamides (**3a–f**) has been synthesized by the condensation of 9-aminoacridine derivatives with benzimidazole or benzoxazole derivatives. Schiff's bases **7a–e(f)**, **9** and **11** were synthesized by microwave irradiation. Compounds **3a–f**, **7a–e(f)** and **11** were evaluated for anti-inflammatory and analgesic activities. Kinase inhibition assays for all these compounds were carried out against CDK-1, CDK-5 and GSK-3.

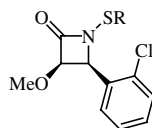
A novel kind of nitrogen heterocycle compound induces apoptosis of human chronic myelogenous leukemia K562 cells

pp 3766–3774

Guoyu Ding, Feng Liu, Ting Yang, Yuyang Jiang,* Hua Fu and Yufen Zhao

Among the novel kind of nitrogen heterocycle compounds synthesized, compound **8**, a potential anti-tumor agent, has the lowest IC₅₀ 20.83 µg/mL, which can induce K562 cell apoptosis through two pathways.

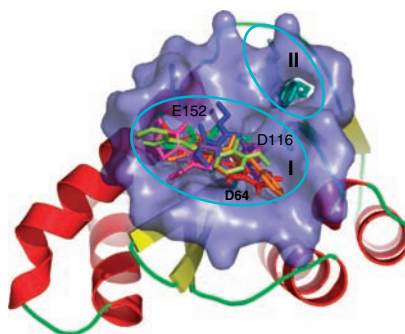


***N*-Thiolated β -lactam antibacterials: Effects of the *N*-organothio substituent on anti-MRSA activity** pp 3775–3784Bart Heldreth, Timothy E. Long, Seyoung Jang, G. Suresh Kumar Reddy, Edward Turos,*
Sonja Dickey and Daniel V. Lim

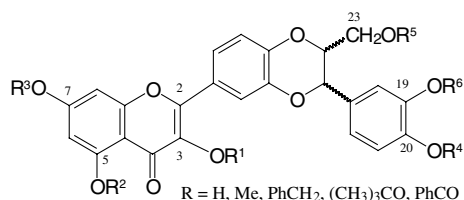
A study on the structure–activity profiles of *N*-thiolated β -lactams are reported which demonstrate the importance of the *N*-organothio moiety on anti-MRSA activity.

Mining the NCI antiviral compounds for HIV-1 integrase inhibitors

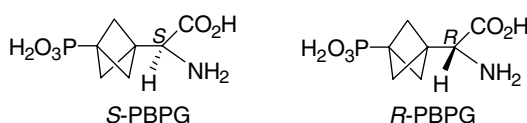
pp 3785–3792

Jinxia Deng, James A. Kelley, Joseph J. Barchi, Tino Sanchez, Raveendra Dayam,
Yves Pommier and Nouri Neamati***New derivatives of silybin and 2,3-dehydrosilybin and their cytotoxic and P-glycoprotein modulatory activity**

pp 3793–3810

Petr Džubák, Marián Hajdúch, Radek Gažák, Alena Svobodová, Jitka Psotová,
Daniela Walterová, Petr Sedmera and Vladimír Křen***Synthesis and biological evaluation of (2*S*)- and (2*R*)-2-(3'-phosphonobicyclo[1.1.1]pentyl)glycines as novel group III selective metabotropic glutamate receptor ligands**

pp 3811–3817

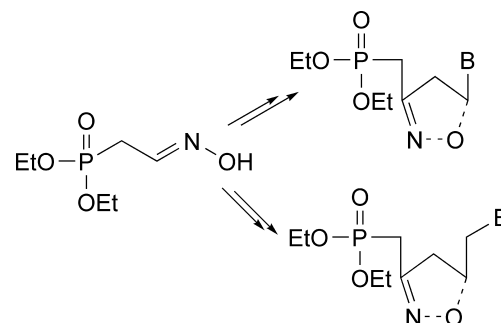
Rosanna Filosa, Maura Marinozzi, Gabriele Costantino, Mette Brunsgaard Hermit,
Christian Thomsen and Roberto Pellicciari*

Synthesis and biological evaluation of phosphonated dihydroisoxazole nucleosides

pp 3818–3824

Giovanni Romeo,* Daniela Iannazzo, Anna Piperno, Roberto Romeo, Monica Saglimbeni, Maria Assunta Chiacchio, Emanuela Balestrieri, Beatrice Macchi and Antonio Mastino

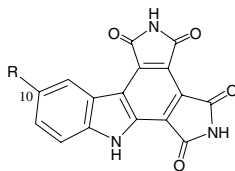
The synthesis of unsaturated phosphonated nucleosides is described starting from a phosphonated oxime.



Synthesis and biological evaluation of new dipyrrolo[3,4-*a*:3,4-*c*]carbazole-1,3,4,6-tetraones, substituted with various saturated and unsaturated side chains via palladium catalyzed cross-coupling reactions

pp 3825–3834

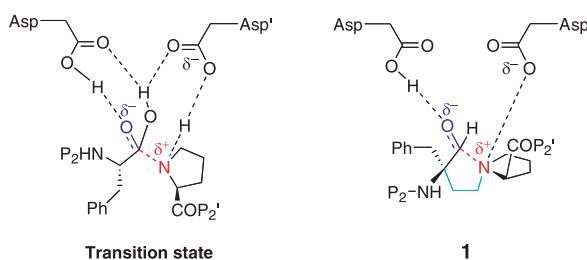
Hélène Hénon, Fabrice Anizon, Roy M. Golsteyn, Stéphane Léonce, Robert Hofmann, Bruno Pfeiffer and Michelle Prudhomme*



An unusual functional group interaction and its potential to reproduce steric and electrostatic features of the transition states of peptidolysis

pp 3835–3847

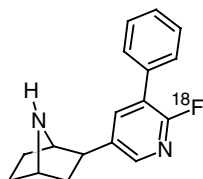
Arnaud Gautier, Delphine Pitrat and Jens Hasserodt*



Synthesis and radiosynthesis of [^{18}F]FPhEP, a novel $\alpha_4\beta_2$ -selective, epibatidine-based antagonist for PET imaging of nicotinic acetylcholine receptors

pp 3848–3858

Gaëlle Roger, Wadad Saba, Héric Valette, Françoise Hinnen, Christine Coulon, Michèle Ottaviani, Michel Bottlaender and Frédéric Dollé*

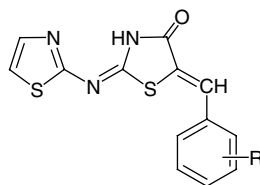


[^{18}F]-1 ([^{18}F]FPhEP)

Synthesis and antimicrobial activity of novel 2-thiazolylimino-5-arylidene-4-thiazolidinones

pp 3859–3864

Paola Vicini,* Athina Geronikaki, Kitka Anastasia, Matteo Incerti and Franca Zani

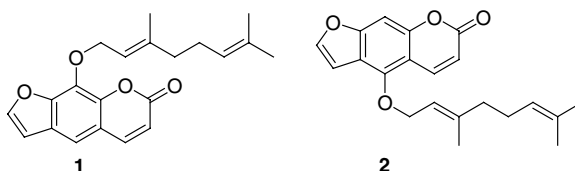


A new series of 2-thiazolylimino-5-arylidene-4-thiazolidinones were synthesized and assayed in vitro for their antimicrobial activity. The designed compounds exhibited a remarkable inhibition of the growth of a wide number of Gram positive bacteria, including penicillin resistant strains, and of Gram negative *Haemophilus influenzae*.

Synthesis of 8-geranyloxypsoralen analogues and their evaluation as inhibitors of CYP3A4

pp 3865–3871

E. C. Row, S. A. Brown, A. V. Stachulski and M. S. Lennard*

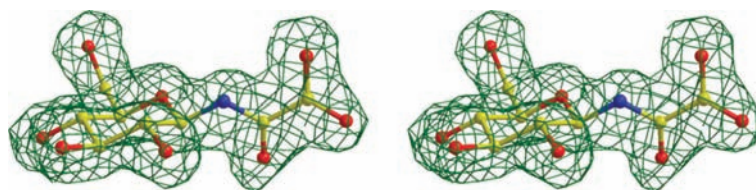


The inhibitory effect of a series of 8-geranyloxypsoralens (**1**), an analogue of the 5-substituted counterpart bergamottin (**2**), on human CYP3A4 activity is described.

Binding of oxalyl derivatives of β -D-glucopyranosylamine to muscle glycogen phosphorylase b

pp 3872–3882

Theodoros Hadjiloi, Costas Tiraidis, Evangelia D. Chrysina, Demetres D. Leonidas, Nikos G. Oikonomakos,* Panagiotis Tsipos and Thanasis Gimisis



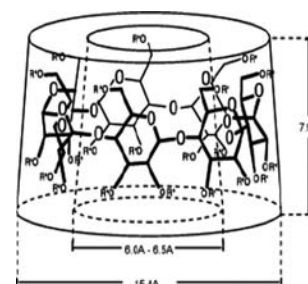
Five oxalyl derivatives of β -D-glucopyranosylamine were tested for inhibition of and binding to glycogen phosphorylase b. The structural basis of inhibition is presented by analysing the crystal structures of the enzyme in complex with the five inhibitors at a resolution of 1.93–1.96 Å.

Thermodynamics of inclusion complexes of natural and modified cyclodextrins with propranolol in aqueous solution at 298 K

pp 3883–3887

Giuseppina Castronuovo* and Marcella Niccoli

Cyclodextrins, cyclic oligosaccharides, present a prevalently hydrophobic cavity. They can form inclusion complexes having 1:1 stoichiometry. The length of the alkyl chain of the guest and the size of the macrocycle mostly determine the kind of forces ruling the association process.

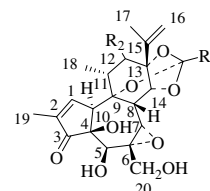


Preparation of yuanhuacine and relative daphne diterpene esters from *Daphne genkwa* and structure–activity relationship of potent inhibitory activity against DNA topoisomerase I

Shixuan Zhang,* Xiaona Li, Fenghong Zhang, Puwen Yang, Xiujuan Gao and Qiling Song

pp 3888–3895

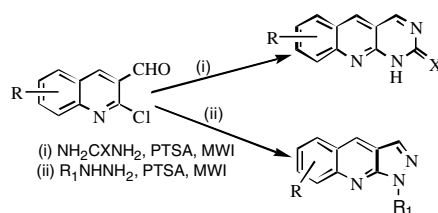
Two new daphne diterpene esters **2** and **4**, together with three known compounds, were isolated from the plant *Daphne genkwa*, and three derivatives were synthesized. These compounds exhibited potent inhibitory activities against DNA topoisomerase I.



Solvent free microwave synthesis and evaluation of antimicrobial activity of pyrimido[4,5-*b*]- and pyrazolo[3,4-*b*]quinolines

Senniappan Thamarai Selvi,* Vetrivel Nadaraj, Sellappan Mohan, Raju Sasi and Manoharan Hema

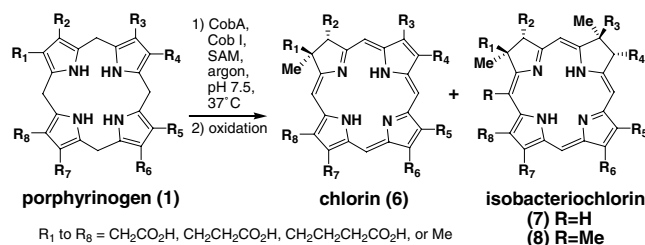
pp 3896–3903



Synthesis of substrate analogs of methyltransferases in the vitamin B₁₂ biosynthetic pathway and characterization of their enzymatic products

Clotilde Pichon-Santander, Patricio J. Santander and A. Ian Scott*

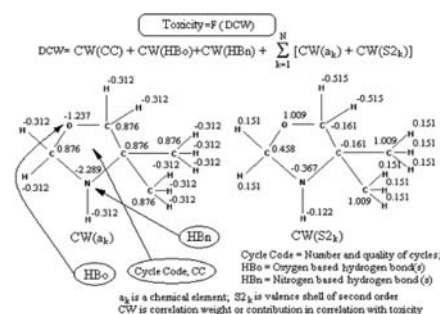
pp 3904–3922



Correlation weighting of valence shells in QSAR analysis of toxicity

Andrey A. Toropov* and Emilio Benfenati

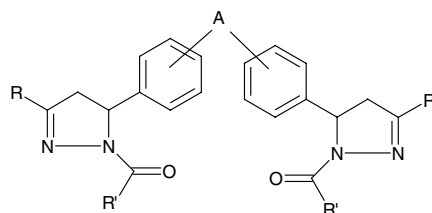
pp 3923–3928



Novel bis(1-acyl-2-pyrazolines) of potential anti-inflammatory and molluscicidal properties

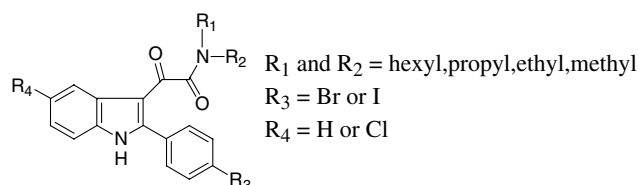
pp 3929–3937

Flora F. Barsoum, Hanaa M. Hosni and Adel S. Girgis*

**Synthesis and in vitro binding of *N,N*-dialkyl-2-phenylindol-3-yl-glyoxylamides for the peripheral benzodiazepine binding sites**

pp 3938–3946

Taryn P. Homes, Filomena Mattner, Paul A. Keller and Andrew Katsifis*



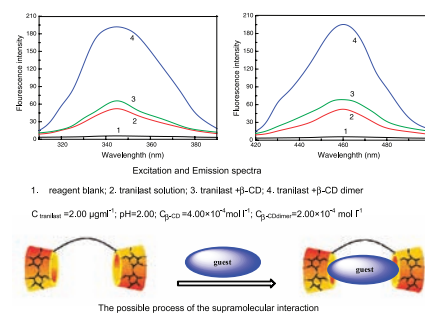
The synthesis of a series of *N,N*-dialkyl-2-phenylindol-3-ylglyoxylamides and their in vitro binding affinities for the peripheral benzodiazepine binding sites and the central benzodiazepine receptors are presented.

Synthesis of ethylenediamine linked β -cyclodextrin dimer and its analytical application for tranilast determination by spectrofluorimetry

pp 3947–3952

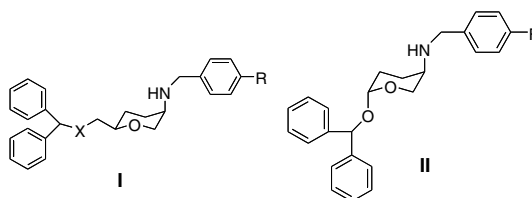
Bo Tang,* Hui-ling Liang, Li-li Tong and Ping Li

Tranilast can give off fluorescence in organic solvent, but it showed a yield in the aqueous solution. When ethylenediamine linked β -CD dimer was added to the aqueous solution of tranilast, ethylenediamine linked β -CD dimer reacted with tranilast to form an inclusion complex, we can observe an obvious increase in fluorescence intensity of tranilast. However, the fluorescence intensity did not obviously enhance when β -CD was added to the aqueous solution of tranilast. So the spectrofluorimetric study of the interaction between ethylenediamine linked β -CD dimer and tranilast was carried out.

**Design, synthesis, and preliminary SAR study of 3- and 6-side-chain-extended tetrahydropyran analogues of *cis*- and *trans*-(6-benzhydryl-tetrahydropyran-3-yl)-benzylamine**

pp 3953–3966

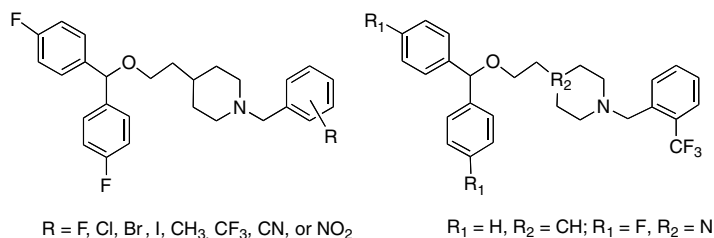
Shijun Zhang, Juan Zhen, Maarten E. A. Reith and Alope K. Dutta*



Structure–activity relationships of substituted *N*-benzyl piperidines in the GBR series: Synthesis of 4-(2-(bis(4-fluorophenyl)methoxy)ethyl)-1-(2-(trifluoromethylbenzyl)piperidine, an allosteric modulator of the serotonin transporter

pp 3967–3973

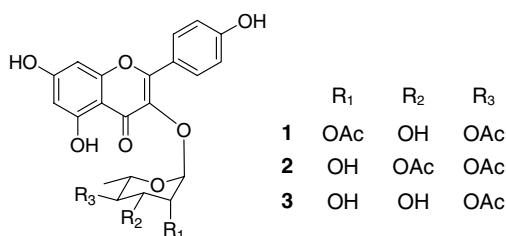
Terrence L. Boos, Elisabeth Greiner, W. Jason Calhoun, Thomas E. Prisinzano, Barbara Nightingale, Christina M. Dersch, Richard B. Rothman, Arthur E. Jacobson and Kenner C. Rice*



Three acetylated flavonol glycosides from *Forsteronia refracta* that specifically inhibit p90 RSK

pp 3974–3977

Ya-ming Xu, Jeffrey A. Smith, Deborah A. Lannigan and Sidney M. Hecht*



OTHER CONTENTS

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*Corresponding author

Supplementary data available via ScienceDirect

COVER

Inhibition of glycogenolysis has been proposed as a therapeutic strategy for the treatment of type 2 diabetes. Members of a novel class of oxalyl derivatives of β -D-glucopyranosylamine were identified as inhibitors of glycogen phosphorylase. The illustration gives a ball-and-stick representation of inhibitors and the lead compound *N*-acetyl- β -D-glucopyranosylamine (shown in red) bound at the catalytic site of the enzyme [Hadjiloi, T.; Tiraidis, C.; Chrysina, E. D.; Leonidas, D. D.; Oikonomakos, N. G.; Tsipos P. and Gimisis T. *Bioorg. Med. Chem.* **2006**, *14*, 3872–3882].

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