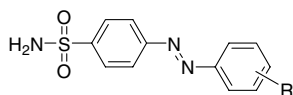


Contents

ARTICLES

- Selective COX-2 inhibitors. Part 1: Synthesis and biological evaluation of phenylazobenzenesulfonamides** pp 4440–4443

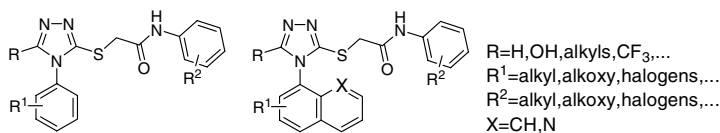
Wei-Jern Tsai, Young-Ji Shiao, Shwu-Jiuan Lin,* Wen-Fei Chiou, Lie-Chwen Lin, Tsang-Hsiung Yang, Che-Ming Teng, Tain-Shung Wu and Li-Ming Yang*



The synthesis, evaluation, and structure–activity relationships of a series of phenylazobenzenesulfonamides as potent and selective COX-2 inhibitors are described.

- Tri-substituted triazoles as potent non-nucleoside inhibitors of the HIV-1 reverse transcriptase** pp 4444–4449

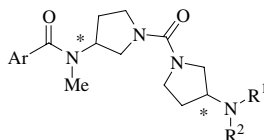
Martha De La Rosa, Hong Woo Kim, Esmir Gunic, Cheryl Jenket, Uyen Boyle, Yung-hyo Koh, Ilia Korboukh, Matthew Allan, Weijian Zhang, Huanming Chen, Wen Xu, Shahul Nilar, Nanhua Yao, Robert Hamatake, Stanley A. Lang, Zhi Hong, Zhijun Zhang and Jean-Luc Girardet*



A new series of 1,2,4-triazoles was synthesized and tested against several NNRTI-resistant HIV-1 isolates containing K103N and/or Y181C mutations or Y188L mutation.

- Synthesis and structure–activity relationships of retro bis-aminopyrrolidine urea (rAPU) derived small-molecule antagonists of the melanin-concentrating hormone receptor-1 (MCH-R1). Part 1** pp 4450–4457

Martin W. Rowbottom,* Troy D. Vickers, Brian Dyck, Jonathan Grey, Junko Tamiya, Mingzhu Zhang, Mehrak Kiankarimi, Dongpei Wu, Wesley Dwight, Warren S. Wade, David Schwarz, Christopher E. Heise, Ajay Madan, Andrew Fisher, Robert Petroski and Val S. Goodfellow*



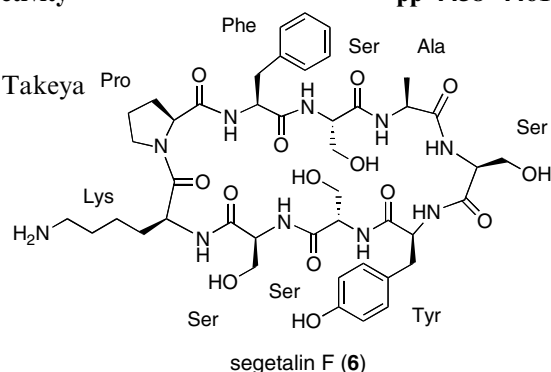
The design, synthesis, and SAR of a series of retro bis-aminopyrrolidine ureas are described. Compounds from this series exhibited potent binding affinity and functional activity at MCH-R1, and good oral bioavailability in rat.

Structure of a new cyclic nonapeptide, segetalin F, and vasorelaxant activity of segetalins from *Vaccaria segetalis*

pp 4458–4461

Hiroshi Morita,* Michiko Eda, Toru Iizuka, Yusuke Hirasawa, Mitsuhiro Sekiguchi, Young Sook Yun, Hideji Itokawa and Koichi Takeya

A new cyclic nonapeptide, segetalin F (**6**), has been isolated from the seeds of *Vaccaria segetalis* and the structure was elucidated by using 2D NMR and chemical means. A series of segetalins showed a vasorelaxant activity against norepinephrine (NE)-induced contractions of rat aorta.

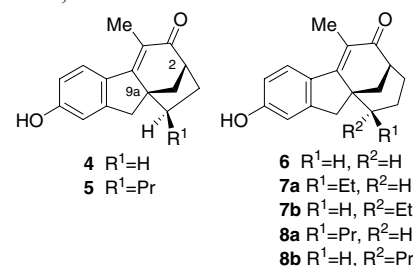


Tetrahydrofluorenones with conformationally restricted side chains as selective estrogen receptor beta ligands

pp 4462–4466

Kenneth J. Wildonger,* Ronald W. Ratcliffe, Ralph T. Mosley, Milton L. Hammond, Elizabeth T. Birzin and Susan P. Rohrer

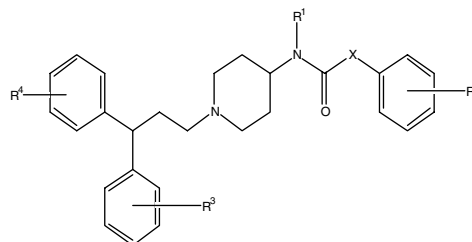
A series of 2-9a bridged tetrahydrofluorenone derivatives were prepared which exhibited significant binding affinity for ER β and high selectivity for ER β over ER α .



Comparative QSAR modeling of CCR5 receptor binding affinity of substituted 1-(3,3-diphenylpropyl)-piperidinyl amides and ureas

pp 4467–4474

J. Thomas Leonard and Kunal Roy*



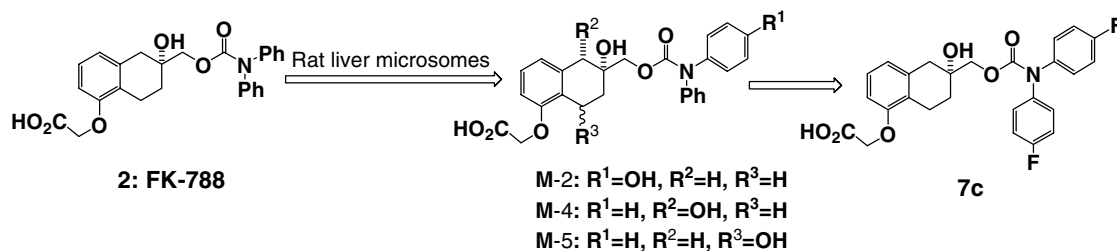
CCR5 binding affinity data of substituted 1-(3,3-diphenylpropyl)-piperidinyl amides and ureas have been subjected to quantitative structure-activity relationship (QSAR) study by linear free energy-related (LFER) model of Hansch using stepwise regression, FA-MLR, FA-PLS, PCRA, GFA-MLR, and G/PLS techniques.



Metabolism investigation leading to novel drug design 2: Orally active prostacyclin mimetics. Part 5

pp 4475–4478

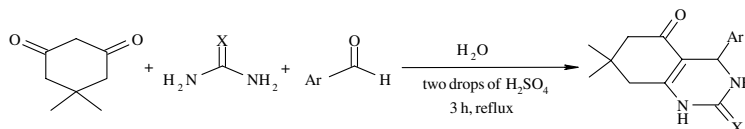
Fujiko Takamura, Akira Tanaka, Hisashi Takasugi, Kiyoshi Taniguchi, Mie Nishio, Jiro Seki and Kouji Hattori*



An efficient one-pot synthesis of octahydroquinazolinone derivatives using catalytic amount of H₂SO₄ in water

pp 4479–4482

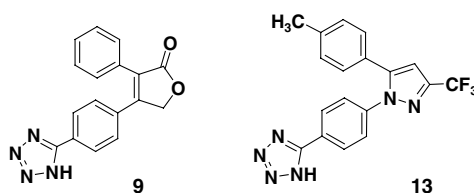
Zahra Hassani, Mohammad Reza Islami* and Maryam Kalantari



Design and synthesis of new water-soluble tetrazolide derivatives of celecoxib and rofecoxib as selective cyclooxygenase-2 (COX-2) inhibitors

pp 4483–4487

Latifeh Navidpour, Mohsen Amini, Hamed Shafaroodi, Khosrou Abdi, Mohammad H. Ghahremani, Ahmad Reza Dehpour and Abbas Shafiee*

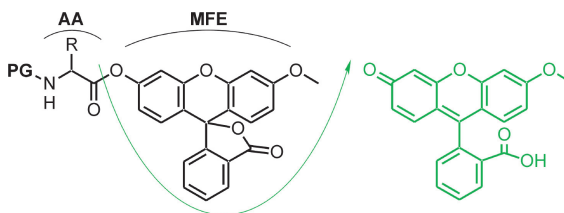


Design, synthesis, and evaluation of a new water-soluble, parenteral COX-2 inhibitor, rofecoxib (**9**) and celecoxib (**13**) analogues, in which the respective SO₂Me and SO₂NH₂ hydrogen-bonding pharmacophores were replaced by a tetrazole ring, are described.

Fluorogenic ester substrates to assess proteolytic activity

pp 4488–4491

Laurent Mugherli, Olga N. Burchak, François Chatelain and Maxim Y. Balakirev*



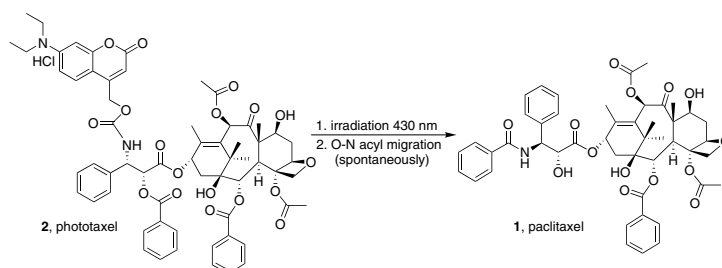
The synthesis of a new type of fluorogenic ester substrates is described. Prepared from fluorescein in three steps with common commercially available precursors, they generate bright green fluorescence upon proteolysis.



Development of first photoresponsive prodrug of paclitaxel

pp 4492–4496

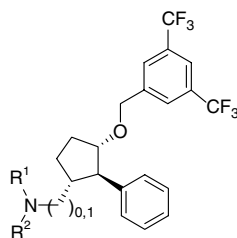
Mariusz Skwarczynski, Mayo Noguchi, Shun Hirota, Youhei Sohma, Tooru Kimura, Yoshio Hayashi* and Yoshiaki Kiso*



Cyclopentane-based human NK1 antagonists. Part 1: Discovery and initial SAR

pp 4497–4503

Paul E. Finke,* Laura C. Meurer, Dorothy A. Levorse, Sander G. Mills, Malcolm MacCoss, Sharon Sadowski, Margaret A. Cascieri, Kwei-Lan Tsao, Gary G. Chicchi, Joseph M. Metzger and D. Euan MacIntyre



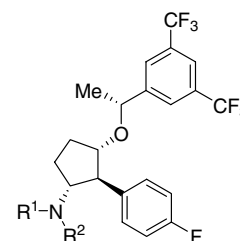
The synthesis and initial SAR of cyclopentane-based hNK1 antagonists is reported.

Cyclopentane-based human NK1 antagonists. Part 2: Development of potent, orally active, water-soluble derivatives

pp 4504–4511

Laura C. Meurer,* Paul E. Finke, Karen A. Owens, Nancy N. Tsou, Richard G. Ball, Sander G. Mills, Malcolm MacCoss, Sharon Sadowski, Margaret A. Cascieri, Kwei-Lan Tsao, Gary G. Chicchi, Linda A. Egger, Silvi Luell, Joseph M. Metzger, D. Euan MacIntyre, Nadia M. J. Rupniak, Angela R. Williams and Richard J. Hargreaves

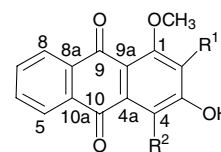
The optimization of a cyclopentane-based hNK1 antagonist scaffold will be discussed in the context of enhanced water-solubility, sub-nanomolar hNK1 binding affinity, and oral activity in two in vivo models.

**Antifungal anthraquinones from *Saprosma fragrans***

pp 4512–4514

D. N. Singh,* N. Verma, S. Raghuwanshi, P. K. Shukla and D. K. Kulshreshtha

A new 3,4-dihydroxy-1-methoxy anthraquinone-2-carboxaldehyde (**1**) together with a known anthraquinone, damnacanthol (**2**) were isolated and characterized by spectroscopic analysis. Compounds (**1**) and (**2**) were found to exhibit antifungal activity against *Trichophyton mentagrophytes* and *Sporitrichum schenckii*.

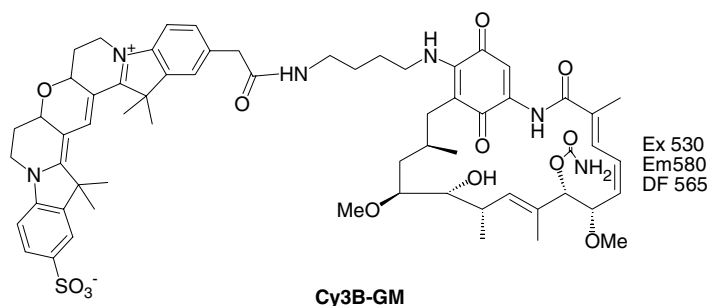


Compound	R ¹	R ²
1	CHO	OH
1R	CH ₂ OH	OH
2	CHO	H

Synthesis of a red-shifted fluorescence polarization probe for Hsp90

pp 4515–4518

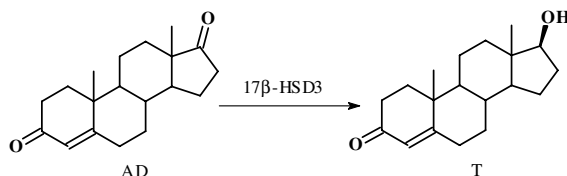
Kamalika Moulick, Cristina C. Clement, Julia Aguirre, Joungnam Kim, Yanlong Kang, Sara Felts and Gabriela Chiosis*



Synthesis, biochemical evaluation and rationalisation of the inhibitory activity of a series of 4-hydroxyphenyl ketones as potential inhibitors of 17 β -hydroxysteroid dehydrogenase type 3 (17 β -HSD3)

pp 4519–4522

Rupinder K. Lota, Sachin Dhanani, Caroline P. Owen* and Sabbir Ahmed*



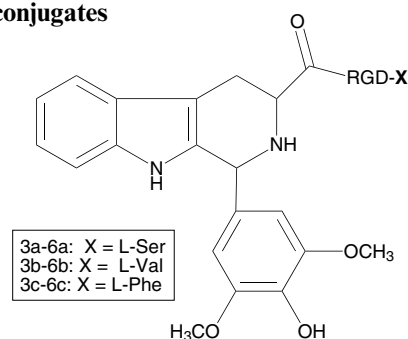
We report the preliminary results of the synthesis and biochemical evaluation of a number of novel inhibitors of type 3 isozyme of the enzyme 17 β -hydroxysteroid dehydrogenase (17 β -HSD3).

Dual-acting agents that possess free radical scavenging and antithrombotic activities: Design, synthesis, and evaluation of phenolic tetrahydro- β -carboline RGD peptide conjugates

pp 4523–4527

Wei Bi,* Lanrong Bi, Jianhui Cai, Sanguang Liu, Shiqi Peng, Nicholas O. Fischer, Jeffrey B.-H. Tok* and Guohua Wang*

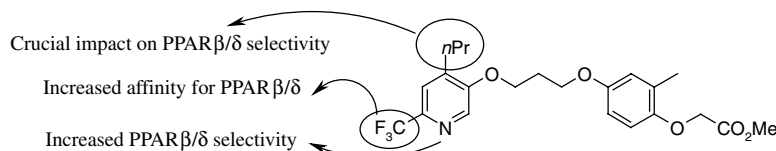
We describe the design and synthesis of dual-acting agents having both free radical scavenging and antithrombotic activities. These compounds may potentially be beneficial in treating myocardial ischemic/reperfusion injuries.



Studies towards the conception of new selective PPAR β/δ ligands

pp 4528–4532

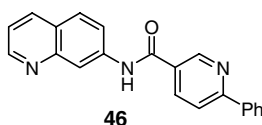
Carine Ekambomé Basséne, Franck Suzenet, Nathalie Hennuyer, Bart Staels, Daniel-Henri Caignard, Catherine Dacquet, Pierre Renard and Gérald Guillaumet*



N-Tetrahydroquinolinyl, N-quinolinyl and N-isoquinolinyl biaryl carboxamides as antagonists of TRPV1

pp 4533–4536

Susan M. Westaway,* Ying-Kit Chung, John B. Davis, Vicky Holland, Jeffrey C. Jerman, Stephen J. Medhurst, Harshad K. Rami, Geoffrey Stemp, Alexander J. Stevens, Mervyn Thompson, Kim Y. Winborn and James Wright

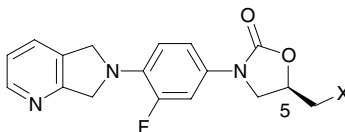


Starting from the high throughput screening hit (3), novel N-tetrahydroquinolinyl, N-quinolinyl and N-isoquinolinyl carboxamides have been identified as potent antagonists of the ion channel TRPV1. The N-quinolinyl nicotinamide (46) showed excellent potency at human, guinea pig and rat TRPV1, a favourable *in vitro* DMPK profile and activity in an *in vivo* model of inflammatory pain.

Antibacterial activity of pyrrolopyridine-substituted oxazolidinones: synthesis and in vitro SAR of various C-5 acetamide replacements

pp 4537–4542

Steven D. Paget, Christine M. Boggs, Barbara D. Foleno, Raul M. Goldschmidt, Dennis J. Hlasta, Michele A. Weidner-Wells, Harvey M. Werblood, Karen Bush and Mark J. Macielag*

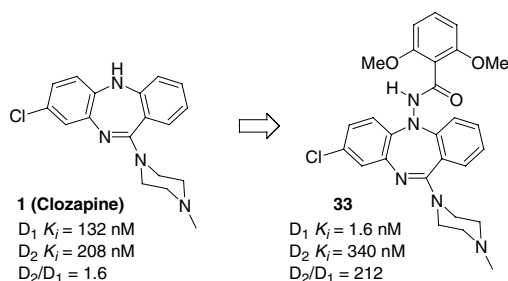


A series of pyrrolopyridine-substituted oxazolidinones containing various C-5 acetamide isosteres was synthesized and the structure–antibacterial activity relationships determined against a representative panel of susceptible and resistant Gram-positive bacteria.

Hydrazides of clozapine: A new class of D₁ dopamine receptor subtype selective antagonists

pp 4543–4547

T. K. Sasikumar,* D. A. Burnett, H. Zhang, A. Smith-Torhan, A. Fawzi and J. E. Lachowicz



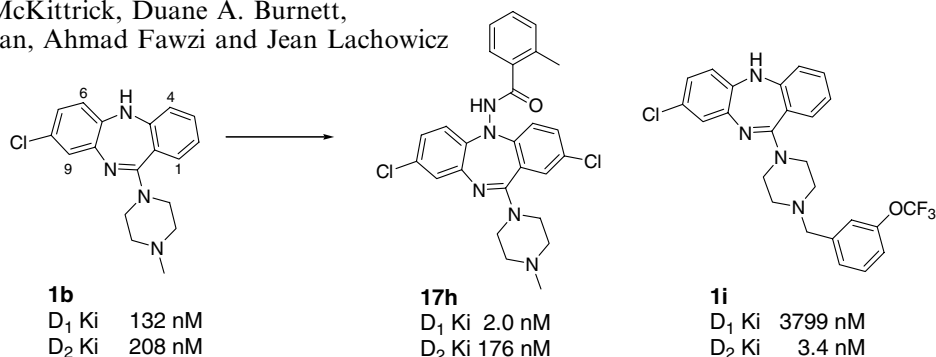
A series of potent and selective dopamine D₁/D₅ antagonists have been discovered based on the clozapine unit.

Modification of the clozapine structure by parallel synthesis

pp 4548–4553

Jing Su,* Haiqun Tang, Brian A. McKittrick, Duane A. Burnett, Hongtao Zhang, April Smith-Torhan, Ahmad Fawzi and Jean Lachowicz

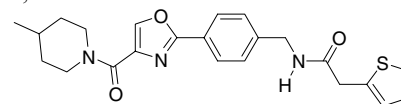
The structure of clozapine was modified to provide two series of compounds that displayed high selectivity for either the dopamine D₁ or D₂ receptor.


Discovery and structure–activity relationship of 2-phenyl-oxazole-4-carboxamide derivatives as potent apoptosis inducers

pp 4554–4558

Vincent W.-F. Tai,* David Sperandio, Emma J. Shelton, Joane Litvak, Keith Pararajasingham, Ben Cebon, Julia Lohman, John Eksterowicz, Seema Kantak, Peter Sabbatini, Cindy Brown, Jennifer Zeitz, Chris Reed, Bill Maske, Doris Graupe, Alberto Estevez, Jason Oeh, Darren Wong, Yong Ni, Paul Sprengeler, Robert Yee, Catherine Magill, Anthony Neri, Sui Xiong Cai, John Drewe, Ling Qiu, John Herich, Ben Tseng, Shailaja Kasibhatla and Jeffrey R. Spencer*

Novel 2-phenyl-oxazole-4-carboxamide-containing apoptosis inducers were discovered from a cell-based assay for caspase-3 activation. Synthesis, in vitro, and in vivo activity profiles are reported.

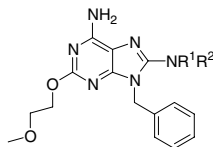
**1a**

$EC_{50} \text{ T47D} = 0.55 \mu\text{M}$
 $EC_{50} \text{ ZR751} = 0.29 \mu\text{M}$
 $EC_{50} \text{ DLD1} = 0.92 \mu\text{M}$

Synthesis and immunostimulatory activity of 8-substituted amino 9-benzyladenines as potent Toll-like receptor 7 agonists

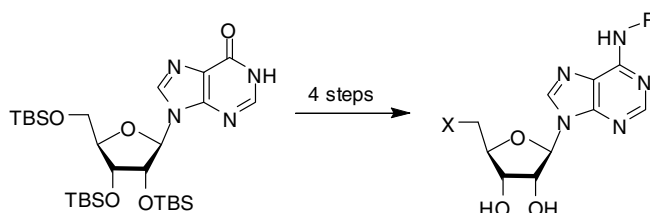
pp 4559–4563

Guangyi Jin, Christina C. N. Wu, Rommel I. Tawatao, Michael Chan, Dennis A. Carson and Howard B. Cottam*

**An expedient synthesis of *N*⁶-substituted-5'-modified adenosines**

pp 4564–4566

T. D. Ashton and Peter J. Scammells*

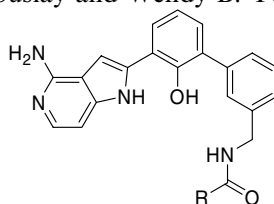


Adenosine analogues which are substituted at *N*⁶ and/or modified at the 5'-position have been the subject of widespread interest. Herein we report a short and efficient synthesis of *N*⁶-substituted 5'-modified adenosines, which was achieved in four steps from 2',3',5'-tris-*O*-(*tert*-butyldimethylsilyl)inosine.

**Potent 4-amino-5-azaindole factor VIIa inhibitors**

pp 4567–4570

Huiyong Hu,* Aleksandr Kolesnikov, Jennifer R. Riggs, Kieron E. Wesson, Robin Stephens, Ellen M. Leahy, William D. Shrader, Paul A. Sprengeler, Michael J. Green, Ellen Sanford, Margaret Nguyen, Erik Gjerstad, Ronnel Cabuslay and Wendy B. Young



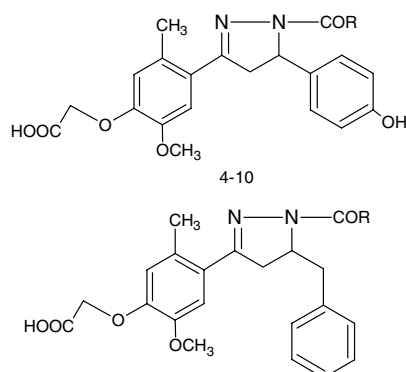
In our continued effort to develop orally bioavailable factor VIIa inhibitors based on the 2-[5-(5-carbamimidoyl-1*H*-benzimidazol-2-yl)-6-hydroxy-biphenyl-3-yl]-succinic acid scaffold, we have identified potent and selective analogs with 4-amino-5-azaindole (1*H*-pyrrolo[3,2-*c*]pyridin-4-ylamine) as a less basic amidine replacement.

Synthesis and evaluation of phenoxy acetic acid derivatives as anti-mycobacterial agents

pp 4571–4574

Mohammad Shahar yar,* Anees Ahmad Siddiqui and Mohamed Ashraf Ali

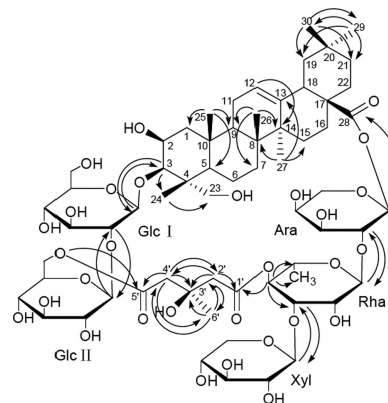
In the present investigation, 2-(4-formyl-2-methoxyphenoxy) acetic acid on condensation with various ketones in methanolic KOH solution yielded the corresponding chalcones (1–3). These corresponding chalcones were reacted with appropriate acid hydrazide in glacial acetic acid leading to the formation of phenoxy acetic acid derivatives. All newly synthesized compounds were evaluated for their anti-mycobacterial activities against *Mycobacterium tuberculosis* H₃₇Rv.



Tubeimoside V (1), a new cyclic bisdesmoside from tubers of *Bolbostemma paniculatum*, functions by inducing apoptosis in human glioblastoma U87MG cells

Guang Cheng, Yun Zhang, Xiang Zhang,* Hai-Feng Tang, Wei-Dong Cao, Da-Kuan Gao and Xi-Ling Wang

Tubeimoside V (1) is a new cyclic bisdesmoside from tubers of *Bolbostemma paniculatum*. Tubeimoside V (1) induced apoptosis in human glioblastoma U87MG cells.

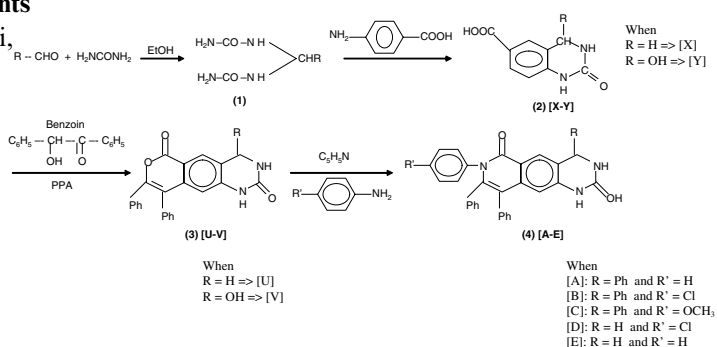


pp 4575–4580

Synthesis and pharmacological study of novel pyrido-quinazoline analogues as anti-fungal, antibacterial, and anticancer agents

Anjani K. Tiwari, A. K. Mishra, Aruna Bajpai, Pushpa Mishra, R. K. Sharma, V. K. Pandey and Vinay Kumar Singh*

A versatile method for novel pyrido-quinazoline analogues as anti-fungal, antibacterial, and anticancer agents is described here. These synthesized compounds were characterized on the basis of spectroscopic techniques and evaluated for specific radiopharmaceuticals.

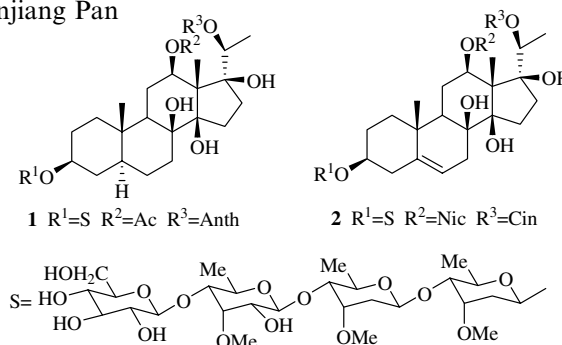


pp 4581–4585

Two novel immunosuppressive pregnane glycosides from the roots of *Stephanotis mucronata*

Yiping Ye,* Fengyang Chen, Hongxiang Sun, Xiaoyu Li and Yuanjiang Pan

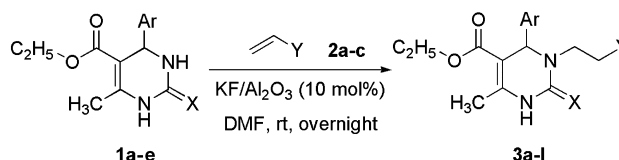
Two novel pregnane glycosides (compounds 1 and 2) were isolated from the roots of *Stephanotis mucronata*. They displayed significant immunosuppressive activities in vitro.



pp 4586–4591

A practical and green approach toward synthesis of N3-substituted dihydropyrimidinones: Using Aza-Michael addition reaction catalyzed by KF/Al₂O₃

Xicun Wang,* Zhengjun Quan, Jun-Ke Wang, Zhang Zhang and Mangang Wang



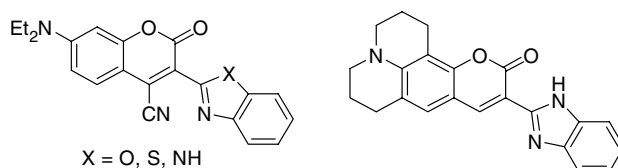
pp 4592–4595

A simple and efficient method for the synthesis of N3-substituted 3,4-dihydropyrimidinones by aza-Michael addition reactions of 3,4-dihydropyrimidinones to α,β -ethylenic compounds catalyzed by KF/Al₂O₃ is described.

Synthesis and anti-angiogenesis activity of coumarin derivatives

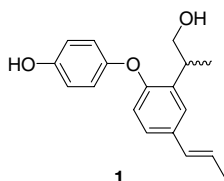
pp 4596–4599

Seokjoon Lee,* Krishnamoorthy Sivakumar, Woon-Seob Shin, Fang Xie and Qian Wang*

**A novel iNOS and COX-2 inhibitor from the aerial parts of *Rodgersia podophylla***

pp 4600–4602

Young-Won Chin, Eun Young Park, Seung-Yong Seo, Kee-Dong Yoon, Mi-Jeong Ahn, Young-Ger Suh, Sang Geon Kim and Jinwoong Kim*

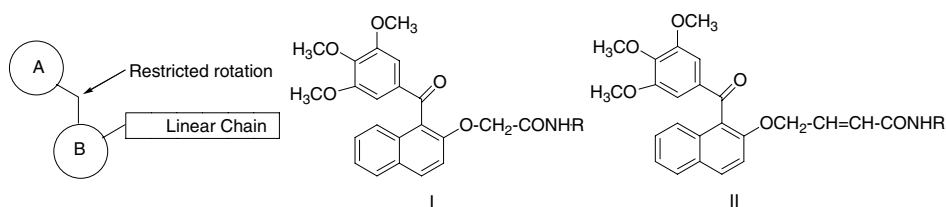


At a concentration of ca. 2 and 3 μ M, rogersinol (1) inhibited 50% of the protein expression of iNOS and COX-2, respectively.

Synthesis of gallic acid based naphthophenone fatty acid amides as cathepsin D inhibitors

pp 4603–4608

Vandana Srivastava, Hari Om Saxena, Karuna Shanker, J. K. Kumar, Suaib Luqman, M. M. Gupta, S. P. S. Khanuja and Arvind S. Negi*



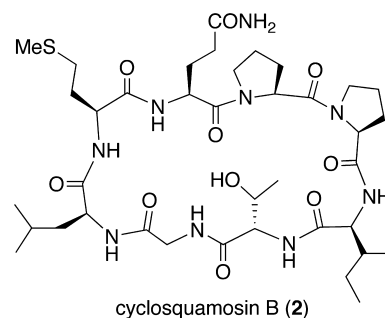
Gallic acid has been modified to naphthophenone fatty acid amide derivatives. The targeted amides had a conformationally restricted pharmacophore and a linear aliphatic chain based on structure and activity relationship of previous studies. Two of the derivatives have shown significant cathepsin D inhibition activity having IC_{50} values 0.056 and 0.136 μ M.

Vasorelaxant activity of cyclic peptide, cyclosquamosin B, from *Annona squamosa*

pp 4609–4611

Hiroshi Morita,* Toru Iizuka, Chee-Yan Choo, Kit-Lam Chan, Koichi Takeya and Jun'ichi Kobayashi

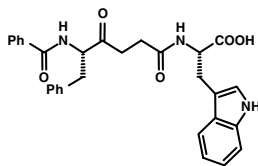
A cyclic octapeptide, cyclosquamosin B (2), isolated from the seeds of *Annona squamosa* showed a vasorelaxant effect on rat aorta. It showed a slow relaxation activity against norepinephrine-induced contractions of rat aorta with/without endothelium. It showed inhibition effect on vasoconstriction of depolarized aorta with high concentration potassium, but moderate inhibition effect on NE-induced contraction in the presence of nicardipine.



Synthesis of novel keto-ACE analogues as domain-selective angiotensin I-converting enzyme inhibitors

pp 4612–4615

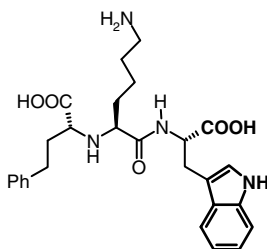
Aloysius T. Nchinda, Kelly Chibale, Pierre Redelinguys and Edward D. Sturrock*



Synthesis and molecular modeling of a lisinopril–tryptophan analogue inhibitor of angiotensin I-converting enzyme

pp 4616–4619

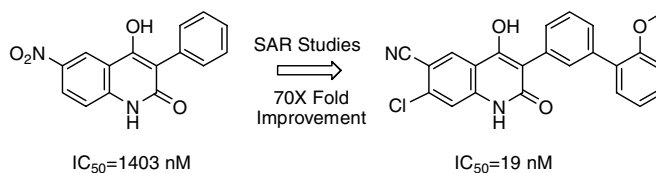
Aloysius T. Nchinda, Kelly Chibale, Pierre Redelinguys and Edward D. Sturrock*



3-Aryl-4-hydroxyquinolin-2(1H)-one derivatives as type I fatty acid synthase inhibitors

pp 4620–4623

Alexey Rivkin,* Yoona R. Kim, Mark T. Goulet, Nathan Bays, Armetta D. Hill, Ilona Kariv, Stefan Krauss, Nicole Ginanni, Peter R. Strack, Nancy E. Kohl, Christine C. Chung, Jeffrey P. Varnerin, Paul N. Goudreau, Amy Chang, Michael R. Tota and Benito Munoz

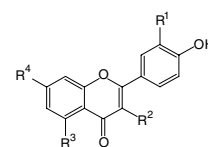


Hepatoprotective activity of *Schouwia thebica* webb

pp 4624–4628

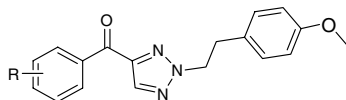
Amani, S. Awaad,* D. J. Maitland and G. A. Soliman

Oral administration of alcoholic extract of *Schouwia thebica* Webb showed that extracts are safe for human use, since it failed to induce death of mice in doses up to 4000 mg/kg body weight. Hepatoprotective activity of the total alcoholic, diethyl ether, chloroform, ethyl acetate and *n*-butanol extracts were tested. It was found that the ethyl acetate and *n*-butanol extracts showed hepatoprotective activity. These extracts significantly reduced the increase in activities of ALT, AST, GGT, levels of glucose, triglycerides and cholesterol in serum of CCl₄ treated rats. The extracts showing hepatoprotective activity were found to contain a new flavonoid chrysoeriol-7-O-β-D-xylopyranoside-(1-2)-arabinofuranoside which was mainly found to be responsible for this activity when tested on lab animals alongside four flavonoids, known as chrysoeriol, Quercetin, quercetin-7-O-rhamnoside and kaempferol-3-O-β-D-glucoside. The structures were established by different spectroscopic techniques.



Synthesis and evaluation of (2-phenethyl-2H-1,2,3-triazol-4-yl)(phenyl)methanones as Kv1. 5 channel blockers for the treatment of atrial fibrillation pp 4629–4632

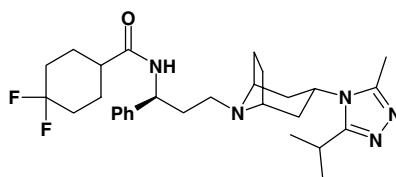
Benjamin E. Blass,* Keith Coburn, Wenlin Lee, Neil Fairweather, Andrew Fluxe, Shengde Wu, John M. Janusz, Michael Murawsky, Gina M. Fadayel, Bin Fang, Michelle Hare, Jim Ridgeway, Ron White, Chris Jackson, Laurent Djandjighian, Richard Hedges, Fred C. Wireko and Amanda L. Ritter



A series of novel (2-phenethyl-2H-1,2,3-triazol-4-yl)(phenyl)methanones were prepared and examined for utility as Kv1. 5 channel blockers for the treatment of atrial fibrillation.

Overcoming HERG affinity in the discovery of the CCR5 antagonist maraviroc pp 4633–4637

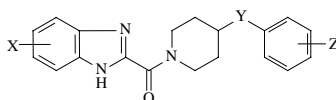
David A. Price,* Duncan Armour, Marcel de Groot, Derek Leishman, Carolyn Napier, Manos Perros, Blanda L. Stammen and Anthony Wood



The discovery of maraviroc **17** is described with particular reference to the generation of high selectivity over affinity for the HERG potassium channel. This was achieved through the use of a high throughput binding assay for the HERG channel that is known to show an excellent correlation with functional effects.

Benzimidazole-2-carboxamides as novel NR2B selective NMDA receptor antagonists pp 4638–4640

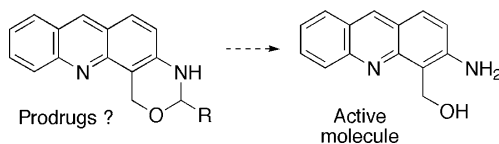
István Borza,* Sándor Kolok, Anikó Gere, József Nagy, László Fodor, Kornél Galgóczy, József Fetter, Ferenc Bertha, Béla Ágai, Csilla Horváth, Sándor Farkas and György Domány



A novel series of benzimidazole-2-carboxamide derivatives was prepared and identified as NR2B selective NMDA receptor antagonists. The influence of some structural elements, like H-bond donor groups placed on the benzimidazole skeleton and the substitution pattern of the piperidine ring, on the biological activity was studied. Compound **6a** showed excellent analgetic activity in the mouse formalin test following po administration.

3,4-Dihydro-1H-[1,3]oxazino[4,5-c]acridines as a new family of cytotoxic drugs pp 4641–4643

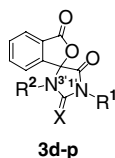
Myriam Ouberaï, Christian Asche, Danièle Carrez, Alain Croisy, Pascal Dumy and Martine Demeunynck*



Synthesis and anticonvulsant activity of new N-1',N-3'-disubstituted-2'H,3H,5'H-spiro-(2-benzofuran-1,4'-imidazolidine)-2',3,5'-triones

pp 4644–4647

Hardik J. Patel, Joe Sarra, Francesco Caruso, Miriam Rossi, Utkarsh Doshi and Ralph A. Stephani*

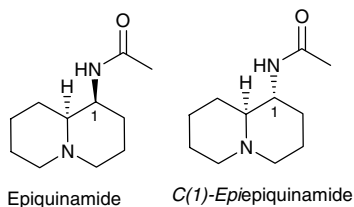


The synthesis and anticonvulsant activity of the new phthalidyl spirohydantoin **3d-p** is reported, **3o** ($R_1 = C_2H_5$, $R_2 = p\text{-NO}_2\text{-C}_6H_4$, $X = O$) $ED_{50} = 41.8 \text{ mg/kg}$.

The synthesis and nicotinic binding activity of (±)-epiquinamide and (±)-C(1)-epiepiquinamide

pp 4648–4651

Akira Kanakubo, Diane Gray, Neal Innocent, Susan Wonnacott and Timothy Gallagher*

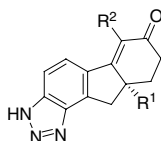


The synthesis of (±)-epiquinamide and (±)-C(1)-epiepiquinamide is reported. In a competition binding assay for [3H]epibatidine binding to rat brain membranes neither ligand showed any significant level of nicotinic activity.


Triazolo-tetrahydrofluorenones as selective estrogen receptor beta agonists

pp 4652–4656

Dann L. Parker, Jr.,* Dongfang Meng, Ronald W. Ratcliffe, Robert R. Wilkening, Donald M. Sperbeck, Mark L. Greenlee, Lawrence F. Colwell, Sherrie Lambert, Elizabeth T. Birzin, Katalin Frisch, Susan P. Rohrer, Stefan Nilsson, Ann-Gerd Thorsell and Milton L. Hammond

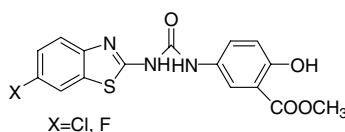


Several tetrahydrofluorenones with a triazole fused across C7–C8 showed high levels of ER β -selectivity and were found to be potent ER β -agonists. As a class they demonstrate improved oral bioavailability in the rat over a parent class of 7-hydroxy-tetrahydrofluorenones. The most selective agonist displayed 5.7 nM affinity and 333-fold selectivity for ER β .

Identification of small-molecule inhibitors of the A β –ABAD interaction

pp 4657–4660

Yuli Xie, Shixian Deng, Zhenzhang Chen, Shidu Yan and Donald W. Landry*

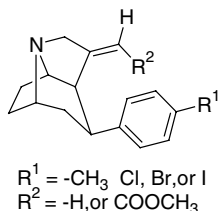


Small molecules that can prevent A β binding to the protein ABAD, a novel strategy for the treatment of Alzheimer's disease, were identified by high-throughput screening and chemical synthesis.

Synthesis and monoamine transporter affinity of front bridged tricyclic 3β-(4'-halo or 4'-methyl)phenyltropanes bearing methylene or carbomethoxymethylene on the bridge to the 2β-position

pp 4661–4663

Fanxing Zeng, Nachwa Jarkas, Michael J. Owens, Clinton D. Kilts, Charles B. Nemeroff and Mark M. Goodman*

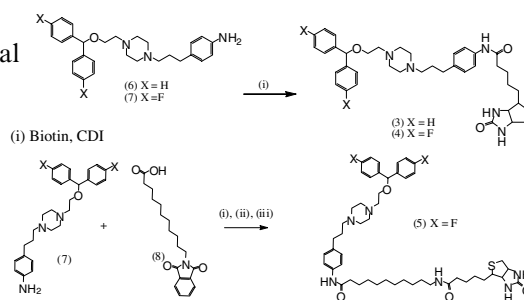


A series of front bridged tricyclic 3β-(4'-halo or 4'-methyl)phenyltropanes bearing methylene or carbomethoxymethylene on the bridge to the 2β-position was synthesized, and their binding affinities to the human monoamine transporters were determined. All compounds studied in this series exhibit a moderate to high potency at all three transporters with SERT or DAT selectivity.

High affinity inhibitors of the dopamine transporter (DAT): Novel biotinylated ligands for conjugation to quantum dots

pp 4664–4667

Ian D. Tomlinson,* John N. Mason, Randy D. Blakely and Sandra J. Rosenthal



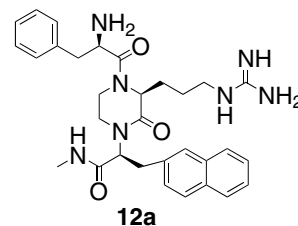
X = F, (i) Method A SOCl₂, CH₂Cl₂; Method B CDI; (ii) (a) Hydrazine, ethanol, (b) CH₂Cl₂; (iii) Biotin, NHS, DCC, DMF

Design and synthesis of potent and selective 1,3,4-trisubstituted-2-oxopiperazine based melanocortin-4 receptor agonists

pp 4668–4673

Xinrong Tian,* Rajesh K. Mishra, Adrian G. Switzer, X. Eric Hu, Nick Kim, Adam W. Mazur, Frank H. Ebetino, John A. Wos, Doreen Crossdoersen, Beth B. Pinney, Julie A. Farmer and Russell J. Sheldon

The design and synthesis of a series of potent 1,3,4-trisubstituted-2-oxopiperazine based MC4 agonists are described. The tripeptidomimetics (**12a,b** and **23**) and the dipeptidomimetic **27** displayed single-nanomolar binding affinity and agonist potency for MC4R and excellent selectivity for MC4R relative to MC1R.

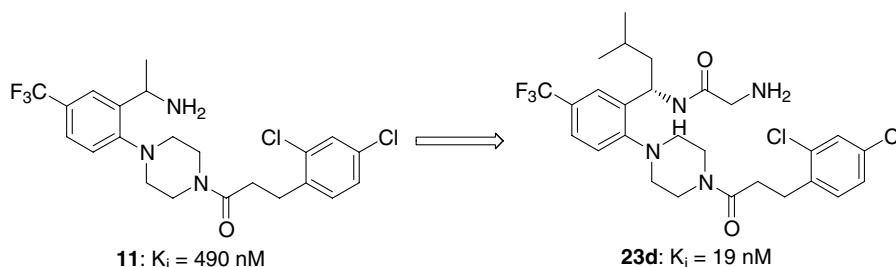


	K _i , nM	EC ₅₀ (E _{max} , %), nM
MC4R	5.7	1.7 (105)
MC1R	659	526(108)

Arylpropionylpiperazines as antagonists of the human melanocortin-4 receptor

pp 4674–4678

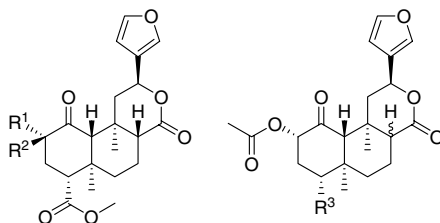
Wanlong Jiang, Fabio C. Tucci, Caroline W. Chen, Melissa Arellano, Joe A. Tran, Nicole S. White, Dragan Marinkovic, Joseph Pontillo, Beth A. Fleck, Jenny Wen, John Saunders, Ajay Madan, Alan C. Foster and Chen Chen*



**Synthesis and in vitro evaluation of salvinorin A analogues:
Effect of configuration at C(2) and substitution at C(18)**

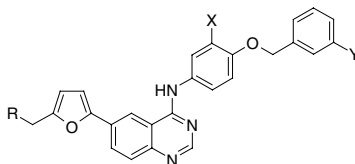
pp 4679–4685

Cécile Béguin,* Michele R. Richards, Jian-Guo Li, Yulin Wang, Wei Xu,
Lee-Yuan Liu-Chen, William A. Carlezon and Bruce M. Cohen


**Optimization and SAR for dual ErbB-1/ErbB-2 tyrosine kinase inhibition in the
6-furanylquinazoline series**

pp 4686–4691

Kimberly G. Petrov, Yue-Mei Zhang, Malcolm Carter, G. Stuart Cockerill, Scott Dickerson,
Cassandra A. Gauthier, Yu Guo, Robert A. Mook, David W. Rusnak, Ann L. Walker, Edgar R. Wood
and Karen E. Lackey*

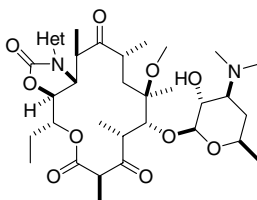


4-(3-Fluorobenzoyloxy)-3-haloanilino provided the best enzyme potency and cellular selectivity. Changes made to the 6-furanyl group had little impact on the enzyme activity, but appeared to dramatically affect the cellular efficacy.


Synthesis and antibacterial activity of C₁₂ des-methyl ketolides

pp 4692–4696

Xiaodong Lin,* Alice C. Rico, Daniel T. Chu, Georgia L. Carroll, Lynn Barker, Ribhi Shawar,
Manoj C. Desai and Jacob J. Plattner

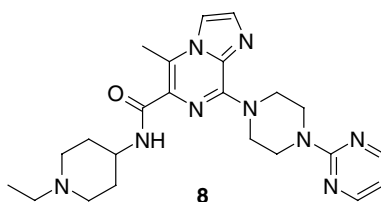


Synthesis of C₁₂ des-methyl ketolides is developed featuring an intramolecular epoxide formation/elimination process to establish the C₁₂ stereocenter. These ketolides are potent against several key respiratory pathogens including resistant strains.


Small molecule inhibitors of IgE synthesis

pp 4697–4699


Alan Brown,* Alan Henderson, Charlotte Lane, Mark Lansdell, Graham Maw and Sandy Monaghan



A novel series of small molecule inhibitors of IgE synthesis was identified and optimized for potency, in vitro metabolic stability and absence of genetic toxicity. Compound **8** showed excellent levels of potency and in vitro metabolic stability.

OTHER CONTENTS**Corrigendum****p 4700****Summary of instructions to authors****p I**

*Corresponding author

 ⁺ Supplementary data available via ScienceDirect**COVER**

View of the crystal structure of the DB819-d(CGCGAATTCGCG)₂ complex, looking down the minor groove of the DNA (see Campbell, N.H.; Evans, D.A.; Lee, M.P.H.; Parkinson, G.N.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2006**, 16, 15). The DB819 molecule is shown in space-filling mode. Visualisation produced with the VMD program. [Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* **1996**, 14, 33.]



Full text of this journal is available, on-line from **ScienceDirect**. Visit www.sciencedirect.com for more information.

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

**ELSEVIER**

ISSN 0960-894X