

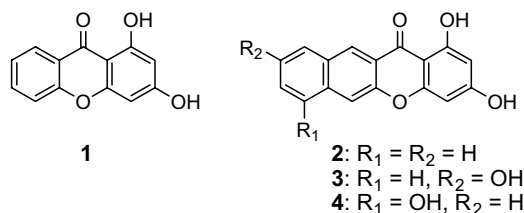
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ARTICLES

Synthesis of xanthone derivatives with extended π -systems as α -glucosidase inhibitors: Insight into the probable binding mode pp 2810–2814

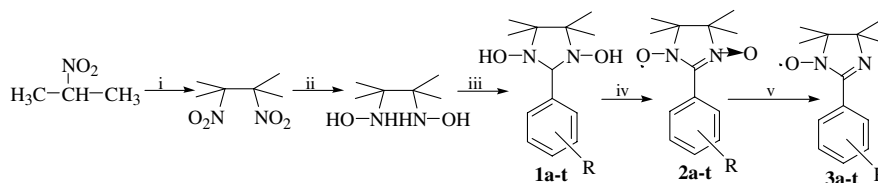
Yan Liu, Lin Ma, Wen-Hua Chen, Bo Wang* and Zun-Le Xu

A series of novel benzoxanthones and their structurally perturbed analogs were synthesized and evaluated as α -glucosidase inhibitors. These compounds exhibited strong inhibitory activities, most probably as a result of the cooperative π -stacking and H-bonding interactions with yeast's α -glucosidase.



Novel 1-oxyl-2-substitutedphenyl-4,4,5,5-tetramethylimidazolines: Synthesis, selectively analgesic action, and QSAR analysis pp 2815–2826

Ming Zhao, Zheng Li, Li Peng, Yu-Rong Tang, Chao Wang, Ziding Zhang* and Shiqi Peng*

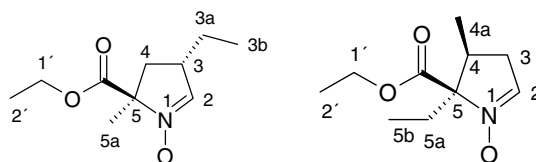


Synthetic route to compounds 3a-t

Twenty novel 1-oxyl-2-substitutedphenyl-4,4,5,5-tetramethylimidazolines (3a–t) were synthesized and characterized as analgesic agents. The preparation, in vivo evaluation, and QSAR analysis of 3a–t were reported.

Free radical trapping properties of several ethyl-substituted derivatives of 5-ethoxycarbonyl-5-methyl-1-pyrroline N-oxide (EMPO) pp 2827–2836

Klaus Stolze,* Natascha Rohr-Udilova, Thomas Rosenau, Andreas Hofinger and Hans Nohl



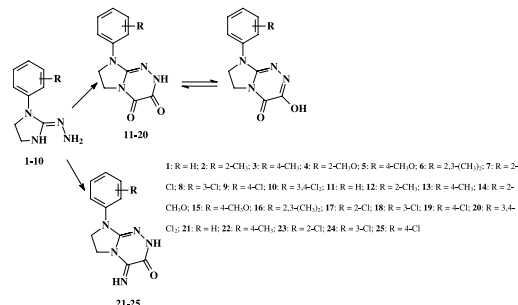
Synthesis and spin trapping properties of a series of EMPO-derived nitrones are reported.

Identification of antitumour activity of novel derivatives of 8-aryl-2,6,7,8-tetrahydroimidazo[2,1-c]-[1,2,4]triazine-3,4-dione and 8-aryl-4-imino-2,3,7,8-tetrahydroimidazo[2,1-c]-[1,2,4]triazine-3(6H)-one

pp 2837–2849

Krzysztof Sztanke,* Kazimierz Pasternak, Jolanta Rzymowska, Małgorzata Sztanke, Martyna Kandefer-Szerszeń, Izabela Dybała and Anna E. Koziół

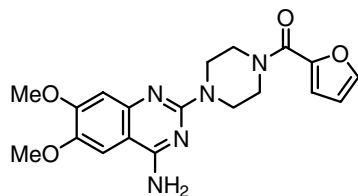
The series of 8-aryl-2,6,7,8-tetrahydroimidazo[2,1-c]-[1,2,4]triazine-3,4-diones (**11–20**) and 8-aryl-4-imino-2,3,7,8-tetrahydroimidazo[2,1-c]-[1,2,4]triazine-3(6H)-ones (**21–25**) were designed and their in vitro cytotoxic activities against human LS180, HeLa, T47D, A549 and RPMI 8226 carcinoma cells are presented. Among them compound **19** revealed a strong affection to LS180 cancer cell line and the efficiency for DNA strand breakage of the examined cancer cell lines. Moreover, imidazotriazin-3,4-dione **20** was able to cause significant viability decreases in human RPMI 8226 peripheral blood myeloma cells. Compound **22** has exhibited remarkable inhibitory effects against LS180 and A549 carcinoma cells, whereas **24** revealed the highest growth inhibition against A549 cell line. Furthermore, the cytotoxic and antibacterial properties of tautomeric 1-aryl-2-hydrazonoimidazolidines (**1–6** and **8–9**), used as building blocks and intermediates in the synthesis of the title classes of compounds are presented. Six of them (**1–2**, **4–6** and **9**) revealed significant antibacterial activities with MIC values in the range of 15.0–78.6 μM . Their activities were compared with those of ampicillin and chloramphenicol.



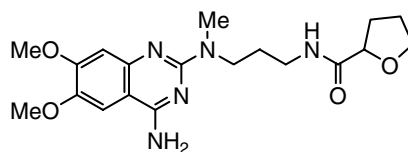
Computational approach to the basicity of a series of α 1-adrenoceptor ligands in aqueous solution

pp 2850–2855

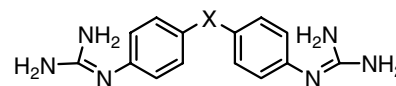
Gemma K. Kinsella, Fernando Rodriguez, Graeme W. Watson and Isabel Rozas*



Prazosin



Alfuzosin



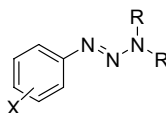
4 (X=NH), **5** (X=CO),
6 (X=CH₂)

The figure illustrates some of the α 1-adrenoceptor ligands object of this study. Their pK_a has been theoretically computed at B3LYP/6-31G* level and the experimental pK_a for some of them has been measured by us.

Antimalarial activity of 1-aryl-3,3-dialkyltriazenes

pp 2856–2859

Keiji Nishiwaki,* Azusa Okamoto, Keizo Matsuo,* Yosuke Kawaguchi, Yoshio Hayase and Katsuaki Ohba

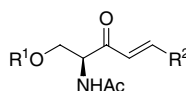


The antimalarial activity of 1-aryl-3,3-dialkyltriazenes to *Plasmodium berghei* NK-65 in infected mice was evaluated at an intraperitoneal dose of 100 mg/kgbw. Some of these compounds were found to possess potent antimalarial activity.

Short-chain 3-ketoceramides, strong apoptosis inducers against human leukemia HL-60 cells

pp 2860–2867

Hideki Azuma,* So Ijichi, Mayuko Kataoka, Akira Masuda, Takayuki Izumi, Tetsuya Yoshimoto and Taro Tachibana



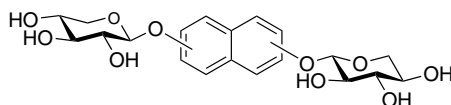
A: $R^1 = \text{H}$, $R^2 = \text{C}_{13}\text{H}_{27}$
B: $R^1 = \text{H}$, $R^2 = \text{CH}=\text{CHC}_{11}\text{H}_{23}$
C: $R^1 = \text{Me}$, $R^2 = \text{C}_{13}\text{H}_{27}$

Three short-chain 3-ketoceramides (compounds **A**, **B**, and **C**) were synthesized and their apoptotic activity against human leukemia HL-60 cells was evaluated.

Synthesis and biology of bis-xylosylated dihydroxynaphthalenes

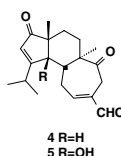
pp 2868–2877

Richard Johnsson, Katrin Mani and Ulf Ellervik*

**Cyathane diterpenes from *Sarcodon cyrneus* and evaluation of their activities of neuritegenesis and nerve growth factor production**

pp 2878–2882

Maria Carla Marcotullio,* Rita Pagiotti, Federica Maltese, Gildas Norbert Oball-Mond Mwankie, Tomohiro Hoshino, Yutaro Obara and Norimichi Nakahata

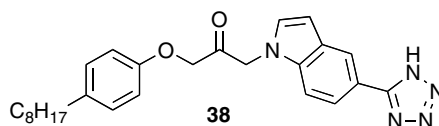


Two new cyathane diterpenes, cyrneine C (**4**) and D (**5**), were isolated from the mushroom *Sarcodon cyrneus*, along with previously isolated cyrneine A, B and glaucopine C. The structures of the novel diterpenoids were determined by the analysis of spectroscopic data. Effects of the cyrneines and glaucopine C on the NGF gene expression in 1321N1 cells were evaluated.

1-(5-Carboxy- and 5-carbamoylindol-1-yl)propan-2-ones as inhibitors of human cytosolic phospholipase A₂α: Bioisosteric replacement of the carboxylic acid and carboxamide moiety

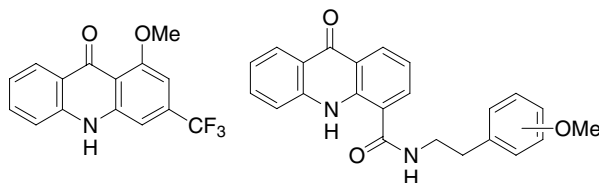
pp 2883–2891

Mark Hess, Alwine Schulze Elfringhoff and Matthias Lehr*

**Acridone derivatives: Design, synthesis, and inhibition of breast cancer resistance protein ABCG2**

pp 2892–2897

Ahcene Boumendjel,* Sira Macalou, Abdelhakim Ahmed-Belkacem, Madeleine Blanc and Attilio Di Pietro

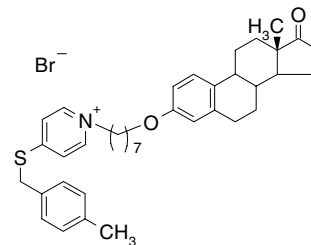


Hybrid molecules of estrone: New compounds with potential antibacterial, antifungal, and antiproliferative activities

pp 2898–2906

J. Adamec,* R. Beckert,* D. Weiß, V. Klimešová,* K. Waisser,
U. Möllmann, J. Kaustová and V. Buchta

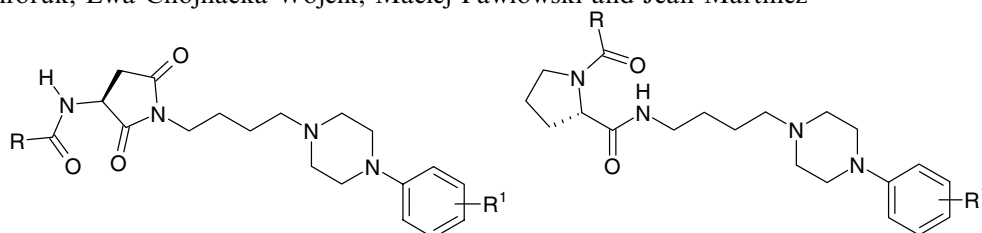
Antibacterial, antifungal, antiproliferative, and cytotoxic activities of series of hybrid molecules of estrone were evaluated and some structure–activity relationships were found. Presence of charge in the molecule seemed to be important for the activity.



Novel class of arylpiperazines containing N-acylated amino acids: Their synthesis, 5-HT_{1A}, 5-HT_{2A} receptor affinity, and in vivo pharmacological evaluation

pp 2907–2919

Paweł Zajdel,* Gilles Subra, Andrzej J. Bojarski, Beata Duszyńska, Ewa Tatarczyńska,
Agnieszka Nikiforuk, Ewa Chojnacka-Wójcik, Maciej Pawłowski and Jean Martinez



R = cyclopentyl, cyclohexyl, norborn-2-ylmethyl, adamantyl
R¹ = *o*-OCH₃, *m*-Cl

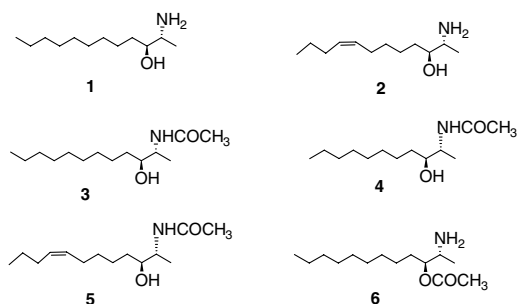


Clavaminols A–F, novel cytotoxic 2-amino-3-alkanols from the ascidian *Clavelina phlegraea*

pp 2920–2926

Anna Aiello, Ernesto Fattorusso,* Antonella Giordano, Marialuisa Menna,
Carmen Navarrete and Eduardo Muñoz


Clavaminols A–F (compounds 1–6) were isolated from the Mediterranean ascidian *Clavelina phlegraea*. Compound 1 was shown to be a cytotoxic compound inducing cell death through activation of the apoptotic machinery.



Quantitative structure–activity relationship of sesquiterpene lactones with cytotoxic activity

pp 2927–2934

Marcus T. Scotti, Mariane B. Fernandes, Marcelo J. P. Ferreira and Vicente P. Emerenciano*

We investigate a set of 37 different sesquiterpene lactones representing 4 skeletons (14 germacranolides, 6 elemanolides, 9 guaianolides and 8 pseudoguaianolides) for their antitumoral properties and the results were submitted to a QSAR study. 

Structure–activity based study of the Smac-binding pocket within the BIR3 domain of XIAP

pp 2935–2943

Aislyn D. Wist,* Lichuan Gu, Stefan J. Riedl, Yigong Shi and George L. McLendon*

A small series of peptide mimics was designed and synthesized to contain a heterocyclic ring in place of the potentially labile N-terminal peptide bond of the tetrapeptide containing the Smac-XIAP-binding motif. The structure–activity relationship between the peptide mimics and XIAP was analyzed in detail. Image shows a surface representation of one peptide mimic, 'AoxSPW', bound to the BIR3 domain of XIAP.

The use of aminoglycoside derivatives to study the mechanism of aminoglycoside 6'-N-acetyltransferase and the role of 6'-NH₂ in antibacterial activity

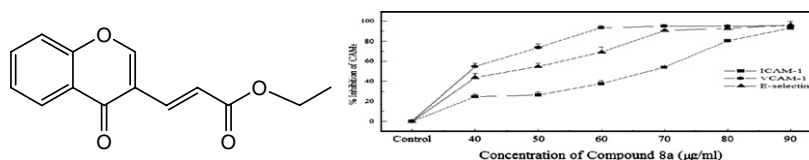
pp 2944–2951

Xuxu Yan, Feng Gao, Sirilata Yotphan, Parseh Bakirtzian and Karine Auclair*

A chromone analog inhibits TNF- α induced expression of cell adhesion molecules on human endothelial cells via blocking NF- κ B activation

pp 2952–2962

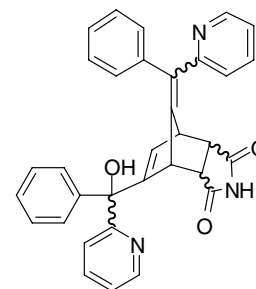
Sarvesh Kumar, Brajendra K. Singh, Anil K. Pandey, Ajit Kumar, Sunil K. Sharma, Hanumantharao G. Raj, Ashok K. Prasad, Erik Van der Eycken, Virinder S. Parmar and Balaram Ghosh*

**Synthesis and activity studies of analogues of the rat selective toxicant norbormide**

pp 2963–2974

David Rennison,* Sergio Bova, Maurizio Cavalli, Fernanda Ricchelli, Alessandra Zulian, Brian Hopkins and Margaret A. Brimble*

A series of NRB-related analogues were prepared to investigate the structural features responsible for, and the in vitro biological markers indicative of, in vivo lethality of the parent molecule in rats.

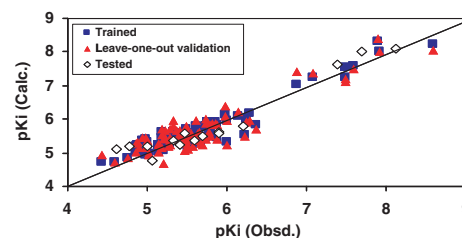


Computational neural network analysis of the affinity of lobeline and tetrabenazine analogs for the vesicular monoamine transporter-2

pp 2975–2992

Fang Zheng, Guangrong Zheng, A. Gabriela Deaciuc, Chang-Guo Zhan, Linda P. Dwoskin and Peter A. Crooks*


Partial least square regression and neural network approaches were used to build linear and nonlinear QSAR models based on a set of 104 tetrabenazine and lobeline analogs that are ligands for the vesicular monoamine transporter-2 (VMAT2). It was demonstrated that a fully interconnected three-layer neural network model trained with the back-propagation procedure could learn the correct relationship between a set of relevant molecular descriptors of the compounds and their $\log(1/K_i)$ values for VMAT2 better than the partial least squares approach.



A conformational transition in the adenylyl cyclase catalytic site yields different binding modes for ribosyl-modified and unmodified nucleotide inhibitors

pp 2993–3002

Jenna L. Wang, Jian-Xin Guo, Qi-Yuan Zhang, Jay J.-Q. Wu, Roland Seifert and Gerald H. Lushington*

A COMBINE-based QSAR model of ribose-substituted nucleotides bound to adenylyl cyclase generated herein correlates well with measured pK_i values, and suggests that ribose substituents may induce a receptor conformational shift. 

Chemical synthesis and biological activities of 16 α -derivatives of 5 α -androstane-3 α ,17 β -diol as antiandrogens

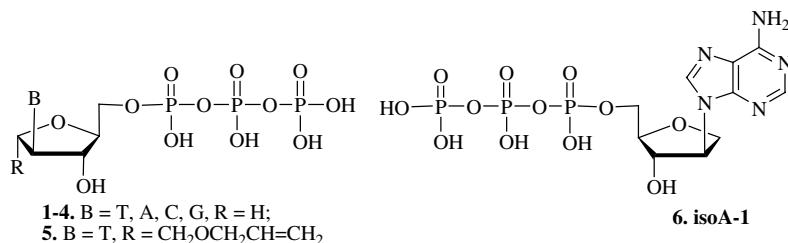
pp 3003–3018

Jenny Roy, Rock Breton, Céline Martel, Fernand Labrie and Donald Poirier*

Synthesis and recognition of novel isonucleoside triphosphates by DNA polymerases

pp 3019–3025

Caiwu Jiang, Bingchao Li, Zhu Guan, Zhenjun Yang,* Liangren Zhang and Lihe Zhang

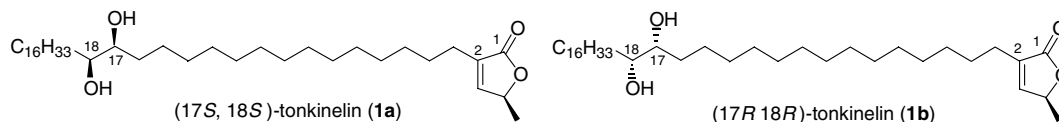


Isonucleoside triphosphates **2** and **6** can be incorporated as substrates into the primer at 3' terminus to lengthen the chain on a DNA template by Vent(exo⁻) and DeepVent(exo⁻) DNA polymerases.

Synthesis, determination of the absolute configuration of tonkinelin, and inhibitory action with bovine heart mitochondrial complex I

pp 3026–3031

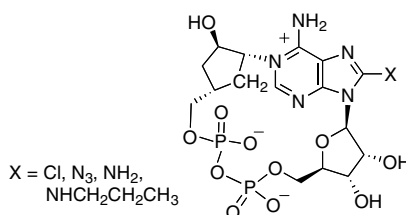
Yasunao Hattori, Hiroyuki Konno, Masato Abe, Hideto Miyoshi, Tetsuhisa Goto and Hidefumi Makabe*



Substitution at the 8-position of 3'-deoxy-cyclic ADP-carbocyclic-ribose, a highly potent Ca²⁺-mobilizing agent, provides partial agonists

pp 3032–3040

Takashi Kudoh, Takashi Murayama, Akira Matsuda and Satoshi Shuto*

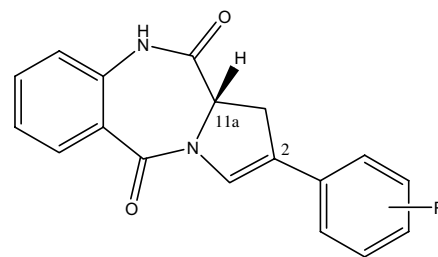


Synthesis of a novel C2-aryl pyrrolo[2,1-*c*][1,4]benzodiazepine-5,11-dione library: Effect of C2-aryl substitution on cytotoxicity and non-covalent DNA binding

pp 3041–3053

Dyeison Antonow, Terence C. Jenkins, Philip W. Howard and David E. Thurston*

A 23-member C2-aryl pyrrolo[2,1-*c*][1,4]benzodiazepine-5,11-dione (PBD dilactam) library has been synthesized using Suzuki coupling, and the effect of base upon racemisation at the C11a-position during the cross-coupling reaction studied. Three library members (**21**, **30** and **33**) were sufficiently cytotoxic in the NCI's preliminary screen to warrant further evaluation, and one (**30**, R = *p*-Br) was found to be cytotoxic at the sub-micromolar level in the A498 renal cancer cell line. DNA thermal denaturation studies suggested that this activity may be associated with non-covalent DNA interaction, and also demonstrated that introduction of C2–C3 unsaturation and addition of C2-aryl functionalities to the PBD dilactam skeleton significantly enhanced helix stabilisation compared to the unsubstituted PBD dilactam (**6**).



Modeling of human ghrelin receptor (hGHS-R1a) in its close state and validation by molecular docking

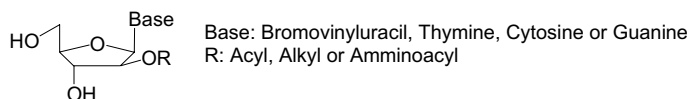
pp 3054–3064

Alessandro Pedretti and Giulio Vistoli*

Novel selective human mitochondrial kinase inhibitors: Design, synthesis and enzymatic activity

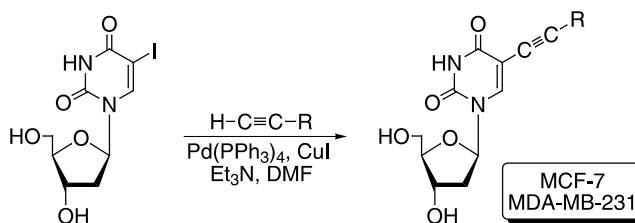
pp 3065–3081

Nunzia Ciliberti, Stefano Manfredini,* Angela Angusti, Elisa Durini,
Nicola Solaroli, Silvia Vertuani, Lisa Buzzoni, Maria Cruz Bonache,
Efrat Ben-Shalom, Anna Karlsson, Ann Saada and Jan Balzarini

**5-Alkynyl-2'-deoxyuridines: Chromatography-free synthesis and cytotoxicity evaluation against human breast cancer cells**

pp 3082–3088

Srinivasarao Meneni, Ingo Ott, Craig D. Sergeant, Adam Sniady, Ronald Gust* and Roman Dembinski*

**Synthesis of 3-[4'-(p-chlorophenyl)-thiazol-2'-yl]-2-[(substituted azetidinone/thiazolidinone)-amino-methyl]-6-bromoquinazolin-4-ones as anti-inflammatory agent**

pp 3089–3096

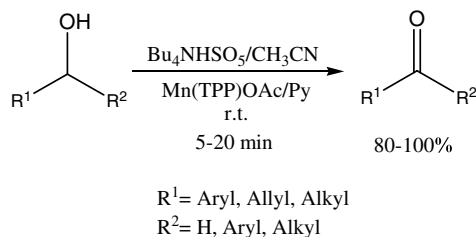
Ashok Kumar,* Chatrasal Singh Rajput and Sudhir Kumar Bhati

Synthesis and characterization of some new bromo-quinazolin-4-one derivatives which have been found to possess anti-inflammatory and analgesic activities. The most active compound is **21**. It shows better anti-inflammatory and analgesic activities at the dose of 100 mg/kg po.

Cytochrome P-450 model reactions: Efficient and highly selective oxidation of alcohols with tetrabutylammonium peroxymonosulfate catalyzed by Mn-porphyrins

pp 3097–3101

Abdolreza Rezaeifard,* Maasoumeh Jafarpour,* Gholamreza Kardan Moghaddam
and Fatemeh Amini



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*Corresponding author

①⁺ Supplementary data available via ScienceDirect**COVER**

Terfenadine (an antihistamine pulled from the market in 1997) bound to a model of an open form of the homo-tetrameric pore domain of hERG, produced using Schrödinger's "Induced Fit Docking" technology [Farid, R.; Day, T.; Friesner, R. A.; Pearlstein, R. A. *Bioorg. Med. Chem.* **2006**, *14*, 3160–3173].

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