

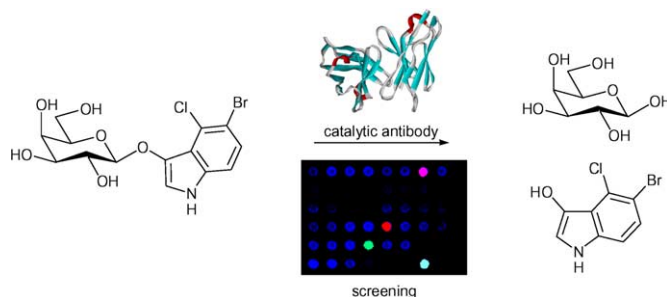
Contents

REVIEW

Catalytic antibodies: hapten design strategies and screening methods

pp 5247–5268

Yang Xu, Noboru Yamamoto and Kim D. Janda*

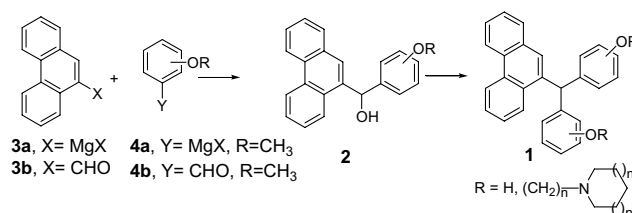


ARTICLES

Diaryloxy methano phenanthrenes: a new class of antituberculosis agents

pp 5269–5276

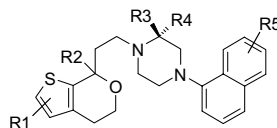
Gautam Panda,* Shagufta, Jitendra Kumar Mishra, Vinita Chaturvedi,
Anil K. Srivastava, Ranjana Srivastava and Brahm S. Srivastava



Novel selective and potent 5-HT reuptake inhibitors with 5-HT_{1D} antagonist activity: chemistry and pharmacological evaluation of a series of thienopyran derivatives

pp 5277–5295

Alicia Torrado,* Carlos Lamas,* Javier Agejas, Alma Jiménez, Nuria Díaz, Jeremy Gilmore,* John Boot,
Jeremy Findlay, Lorna Hayhurst, Louise Wallace, Richard Broadmore and Rosemarie Tomlinson

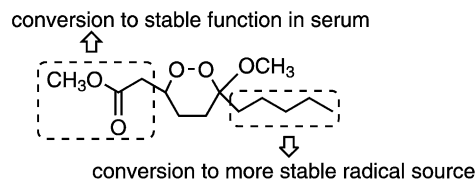


The synthesis and in vitro activity of a novel series of thienopyran derivatives is described. The compounds exhibit dual potency as 5-HT reuptake inhibitors and 5-HT_{1D} antagonists, and feature desirable selectivity with respect to 5-HT_{1B}, α_1 and D₂.

Structure–activity relationship of anti-malarial spongean peroxides having a 3-methoxy-1,2-dioxane structure

pp 5297–5307

Motoyuki Kawanishi, Naoyuki Kotoku, Sawako Itagaki, Toshihiro Horii and Motomasa Kobayashi*

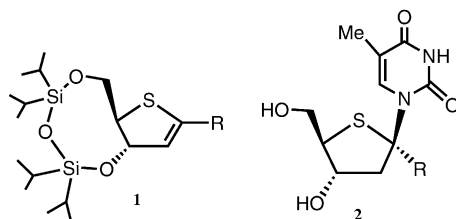


In order to study the structure–activity relationship of anti-malarial spongean peroxides, several analogues concerning with the 6-methoxyacetyl moiety and the 3-pentyl residue in methyl 2-(3-methoxy-3-pentyl-1,2-dioxan-6-yl)acetate were synthesized and evaluated for anti-malarial activity.

Synthesis and antiviral activities of 1'-carbon-substituted 4'-thiothymidines

pp 5309–5316

Kazuhiro Haraguchi,* Haruhiko Takahashi, Hiromichi Tanaka, Hiroyuki Hayakawa, Noriyuki Ashida, Takao Nitanda and Masanori Baba



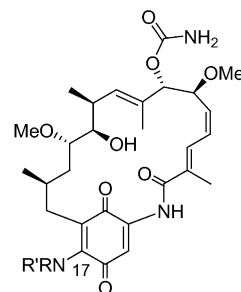
Novel 1'-carbon-substituted 4'-thiothymidines **2** have been synthesized from 1-substituted 4-thiofuranoid glycals **1**. Anti-HSV and anti-HIV activities of these nucleoside analogues were examined.

Synthesis and biological activities of novel 17-aminogeldanamycin derivatives

pp 5317–5329

Zong-Qiang Tian,* Yaoquan Liu, Dan Zhang, Zhan Wang, Steven D. Dong, Christopher W. Carreras, Yiqing Zhou, Giulio Rastelli, Daniel V. Santi and David C. Myles

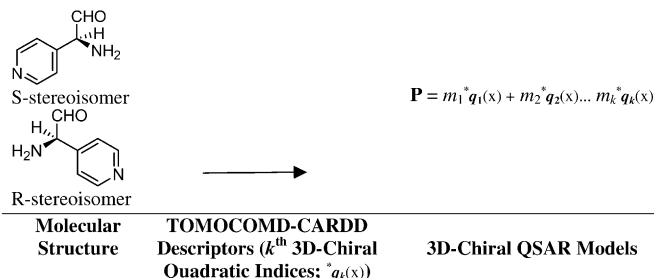
A library of over sixty 17-alkylamino-17-demethoxygeldanamycin were synthesized. Their affinity for Hsp90, ability to inhibit growth of SKBr3 mammalian cells, and in selected cases, water solubility, were measured. The structure–activity relationships of binding affinity to Hsp90 and cytotoxicity in SKBr3 cells are discussed.



3D-Chiral quadratic indices of the 'molecular pseudograph's atom adjacency matrix' and their application to central chirality codification: classification of ACE inhibitors and prediction of σ -receptor antagonist activities

pp 5331–5342

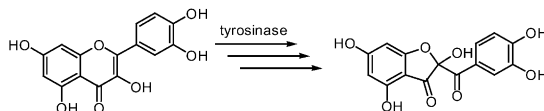
Yovani Marrero Ponce,* Humberto González Díaz, Vicente Romero Zaldivar, Francisco Torrens and Eduardo A. Castro



Oxidation products of quercetin catalyzed by mushroom tyrosinase

pp 5343–5347

Isao Kubo,* Ken-ichi Nihei and Kuniyoshi Shimizu

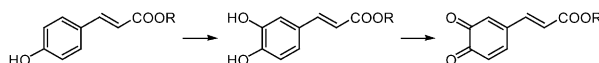


Quercetin was oxidized as a substrate catalyzed by mushroom tyrosinase to the corresponding *o*-quinone and subsequent isomerization to *p*-quinone methide type intermediate; followed by the addition of water on C-2 yielding a relatively stable intermediate, 2-(3,4-dihydroxybenzoyl)-2,4,6-trihydroxy-3(2*H*)-benzofuranone.

Methyl *p*-coumarate, a melanin formation inhibitor in B16 mouse melanoma cells

pp 5349–5354

Isao Kubo,* Ken-ichi Nihei and Kazuo Tsujimoto



p-Coumaric acid and methyl *p*-coumarate inhibit the oxidation of L-tyrosine catalyzed by mushroom tyrosinase. However, both were oxidized as monophenol substrate analogues at an extremely slow rate. Methyl *p*-coumarate significantly suppressed the melanin formation in B16 mouse melanoma cells, whereas *p*-coumaric acid did not show this activity.

Precise structural elucidation of dehydroaltenusin, a specific inhibitor of mammalian DNA polymerase α

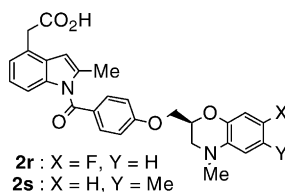
pp 5355–5359

Shinji Kamisuki, Shunya Takahashi, Yoshiyuki Mizushina, Kengo Sakaguchi, Tadashi Nakata and Fumio Sugawara*

**Discovery of a new class of potent, selective, and orally active prostaglandin D₂ receptor antagonists**

pp 5361–5378

Kazuhiko Torisu,* Kaoru Kobayashi, Maki Iwahashi, Yoshihiko Nakai, Takahiro Onoda, Toshihiko Nagase, Isamu Sugimoto, Yutaka Okada, Ryoji Matsumoto, Fumio Nanbu, Shuichi Ohuchida, Hisao Nakai and Masaaki Toda

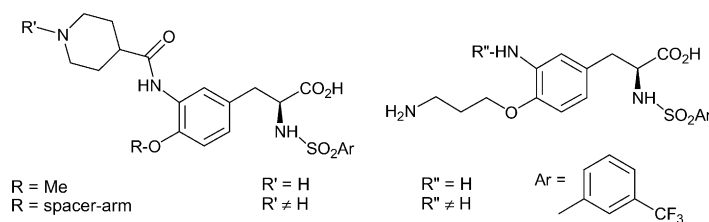


N-(*p*-Alkoxy)benzoyl-2-methylindole-4-acetic acids **2r** and **2s** were identified as a new class of orally active prostaglandin D₂ (PGD₂) receptor antagonists.

Novel RGD-like molecules based on the tyrosine template: design, synthesis and biological evaluation on isolated integrins $\alpha_V\beta_3/\alpha_{IIb}\beta_3$ and in cellular adhesion tests

pp 5379–5393

Stephane Biltresse, Mireille Attolini, Georges Dive, Alex Cordi, Gordon C. Tucker and Jacqueline Marchand-Brynaert*


Theoretical study of gas-phase acidity, pK_a , lipophilicity, and solubility of some biologically active sulfonamides

pp 5395–5403

Milan Remko* and Claus-Wilhelm von der Lieth

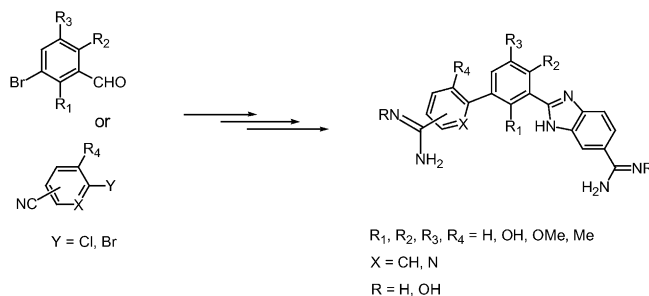


Acidity, pK_a , lipophilicity, and solubility of 19 biologically active substituted sulfonamides (including clinically useful acetazolamide, methazolamide, ethoxzolamide, dichlorophenamide, dorzolamide, and brinzolamide) have been theoretically determined.

Dicationic biphenyl benzimidazole derivatives as antiprotozoal agents

pp 5405–5413

Mohamed A. Ismail, Reto Brun, Tanja Wenzler, Farial A. Tanious, W. David Wilson and David W. Boykin*


Orally active factor Xa inhibitor: synthesis and biological activity of masked amidines as prodrugs of novel 1,4-diazepane derivatives

pp 5415–5426

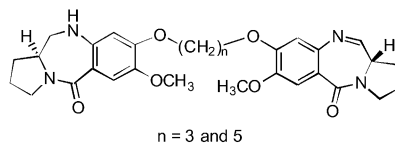
Hiroyuki Koshio,* Fukushi Hirayama, Tsukasa Ishihara, Hiroyuki Kaizawa, Takeshi Shigenaga, Yuta Taniuchi, Kazuo Sato, Yumiko Moritani, Yoshiyuki Iwatsuki, Toshio Uemura, Seiji Kaku, Tomihisa Kawasaki, Yuzo Matsumoto, Shuichi Sakamoto and Shin-ichi Tsukamoto

To improve their anticoagulant activity after oral administration, prodrug strategy was applied to fXa inhibitors based on a 1,4-diazepane template by conversion of the amidine group into amidoxime and alkoxy carbonyloxyamidine groups. This study revealed that amidoxime prodrugs bearing an ester moiety are efficient for the expression of oral anticoagulant activity.

Design, synthesis, and evaluation of mixed imine–amine pyrrolobenzodiazepine dimers with efficient DNA binding affinity and potent cytotoxicity

pp 5427–5436

Ahmed Kamal,* G. Ramesh, O. Srinivas, P. Ramulu, N. Laxman, Tasneem Rehana, M. Deepak, M. S. Achary and H. A. Nagarajaram

**Enantioselective syntheses of (*R*)- and (*S*)-argentilactone and their cytotoxic activities against cancer cell lines**

pp 5437–5442

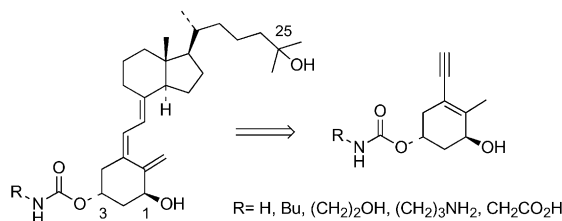
Ângelo de Fatima, Luciana Konecny Kohn, Márcia Aparecida Antônio, João Ernesto de Carvalho and Ronaldo Aloise Pilli*

Concise total syntheses of (*R*)- and (*S*)-argentilactone have been developed via enantioselective catalytic allylation (ECA) and ring-closing metathesis pathways. Both enantiomers were obtained in four steps and 39% overall yield and 82–84% ee from 2-octynal. In addition, we present the results of in vitro activity of (*R*)- and (*S*)-argentilactone against cancer cell line.

**Chemoenzymatic synthesis and biological evaluation of C-3 carbamate analogues of 1 α ,25-dihydroxyvitamin D₃**

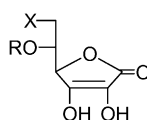
pp 5443–5451

Vicente Gotor-Fernández, Susana Fernández, Miguel Ferrero, Vicente Gotor,* Roger Bouillon and Annemieke Verstuyf

**Design, synthesis and in vitro evaluation on HRPE cells of ascorbic and 6-bromoascorbic acid conjugates with neuroactive molecules**

pp 5453–5463

Stefano Manfredini,* Silvia Vertuani, Barbara Pavan, Federica Vitali, Martina Scaglianti, Fabrizio Bortolotti, Carla Biondi, Angelo Scatturin, Puttur Prasad and Alessandro Dalpiaz

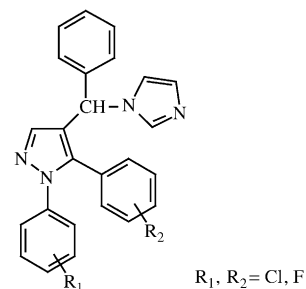


R = OH, *R,S*- or *R*- and *S*-nipecotyl, kynurenyl, diclofenamyl
X = Br, OR


Synthesis, antimicrobial activity and molecular modeling studies of halogenated 4-[1*H*-imidazol-1-yl(phenyl)methyl]-1,5-diphenyl-1*H*-pyrazoles**pp 5465–5483**

Giulia Menozzi,* Luisa Merello, Paola Fossa, Silvia Schenone, Angelo Ranise, Luisa Mosti, Francesco Bondavalli, Roberta Loddo, Chiara Murgioni, Valeria Mascia, Paolo La Colla* and Elena Tamburini

Halogenated diphenylpyrazole analogues of bifonazole were prepared and their microbiological properties were investigated.

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*Corresponding author

 Supplementary data available via ScienceDirect

COVER

The cover image displays a sculpture on The Scripps Research Institute campus, entitled ‘The Flame of Knowledge’. This statue was dedicated in memory of our colleague Norton B. Gilula, the first dean of the graduate program at TSRI and chair of the Department of Cell Biology, and was created by John Safer. The molecules surrounding the statue represent a variety of catalytic antibody substrates and products.

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