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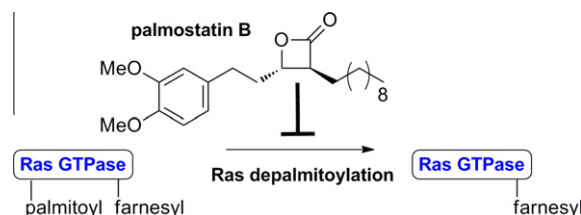
Bioorganic & Medicinal Chemistry Volume 19, Issue 4, 2011

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PERSPECTIVE

Small molecule inhibition of protein depalmitoylation as a new approach towards downregulation of oncogenic Ras signalling pp 1376–1380

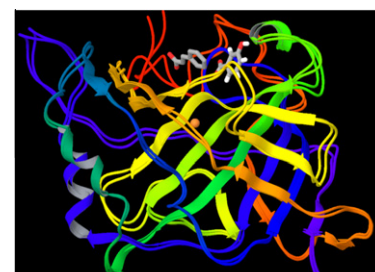
Frank J. Dekker*, Christian Hedberg



ARTICLES

Kinetic and docking studies of phenol-based inhibitors of carbonic anhydrase isoforms I, II, IX and XII evidence a new binding mode within the enzyme active site pp 1381–1389

Serdar Durdagi, Murat Şentürk*, Deniz Ekin, Halis Türker Balaydın, Süleyman Göksu, Ö. İrfan Küfrevioğlu, Alessio Innocenti, Andrea Scozzafava, Claudiu T. Supuran*

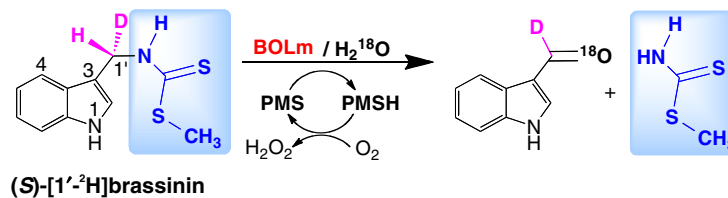


hCA II – 1,3-dimethoxybenzene adduct

Brassinin oxidase mediated transformation of the phytoalexin brassinin: Structure of the elusive co-product, deuterium isotope effect and stereoselectivity

pp 1390–1399

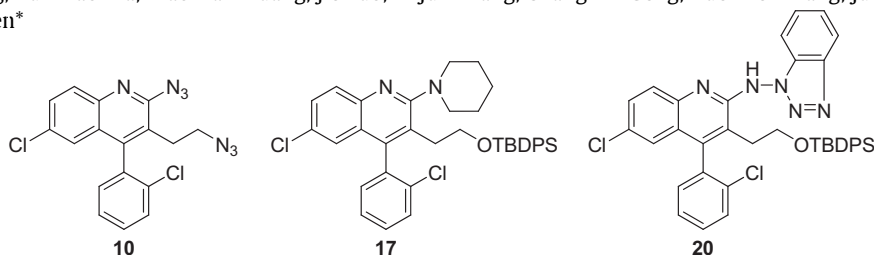
M. Soledade C. Pedras*, Zoran Minic, Vijay K. Sarma-Mamillapalle



Synthesis and biological assay of 4-aryl-6-chloro-quinoline derivatives as novel non-nucleoside anti-HBV agents

pp 1400–1408

Rui-Hua Guo, Quan Zhang, Yun-Bao Ma, Xiao-Yan Huang, Jie Luo, Li-Jun Wang, Chang-An Geng, Xue-Mei Zhang, Jun Zhou, Zhi-Yong Jiang, Ji-Jun Chen*

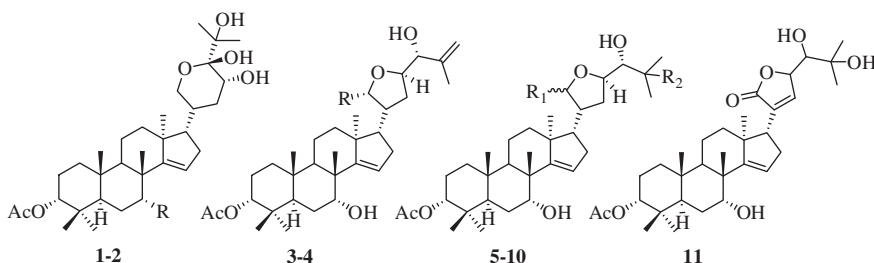


A series of non-nucleoside 4-aryl-6-chloro-quinoline derivatives were synthesized and evaluated for their anti-hepatitis B virus (HBV) activity in HepG2.2.15 cells. Most of the compounds exhibited moderate inhibitory activity against the secretion of HBsAg and HBeAg. Nine compounds (**3**, **5**, **6**, **7**, **10**, **14**, **17**, **20**, **24**) showed significant inhibition against HBV DNA replication with IC_{50} values in the range of 4.4–9.8 μ M. Of them, compounds **10**, **17**, and **20** had low cytotoxicities, resulting in high SI values, >551.2, >143.7, and >284.5, respectively.

Chisopanins A–K, 11 new protolimonoids from *Chisocheton paniculatus* and their anti-inflammatory activities

pp 1409–1417

Ming-Hua Yang, Jun-Song Wang, Jian-Guang Luo, Xiao-Bing Wang, Ling-Yi Kong*

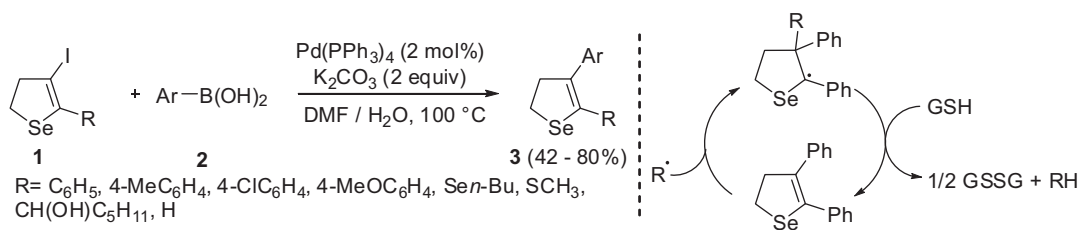


Motivated by positive anti-inflammatory test of crude extracts, 11 new and 13 known protolimonoids were isolated from *Chisocheton paniculatus*. Most protolimonoids showed potent inhibitory activities on LPS-stimulated NO and TNF- α release of RAW 264.7 in vitro.

**The potential antioxidant activity of 2,3-dihydroselenophene, a prototype drug of 4-aryl-2,3-dihydroselenophenes**

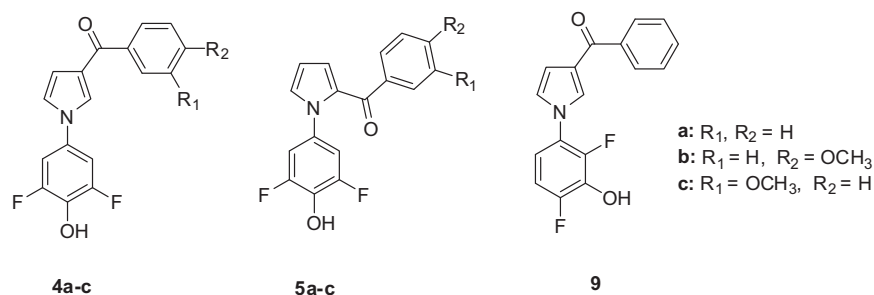
pp 1418–1425

Ricardo F. Schumacher, Alisson R. Rosário, Ana C. G. Souza, Carmine I. Acker, Cristina W. Nogueira, Gilson Zeni*

**Structure–activity relations on [1-(3,5-difluoro-4-hydroxyphenyl)-1H-pyrrol-3-yl]phenylmethanone. The effect of methoxy substitution on aldose reductase inhibitory activity and selectivity**

pp 1426–1433

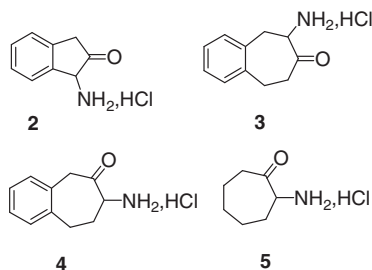
Maria Chatzopoulou, Eduard Mamadou, Maria Juskova, Cathrine Koukoulitsa, Ioannis Nicolaou*, Milan Stefek, Vassilis J. Demopoulos*



Amino-benzosuberone: A novel warhead for selective inhibition of human aminopeptidase-N/CD13

pp 1434–1449

Sébastien Albrecht, Mira Al-Lakkis-Wehbe, Alban Orsini, Albert Defoin*, Patrick Pale, Emmanuel Salomon, Céline Tarnus*, Jean-Marc Weibel

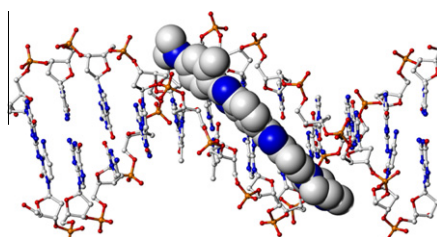


Racemic aminoindanone **2**, amino benzosuberones **3**, **4**, and aminocycloheptanone **5** were synthesised and evaluated as inhibitors of four representative members of zinc-dependent aminopeptidases. K_i values in the low micromolar range against 'one zinc' aminopeptidases are obtained. The stability of these compounds was studied.

Modelling topoisomerase I inhibition by minor groove binders

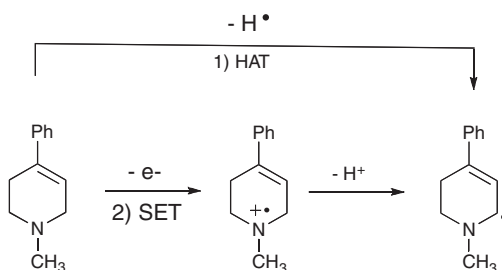
pp 1450–1457

David Winkler*

**Reaction of benzophenone triplet with aliphatic amines. What a potent neurotoxin can tell us about the reaction mechanism**

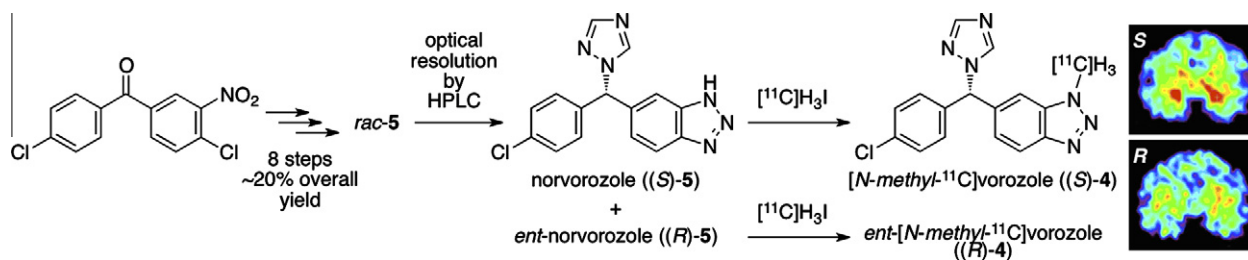
pp 1458–1463

Michelle L. Grimm, William J. Allen, Meghan Finn, Neal Castagnoli Jr., James M. Tanko*

**Practical synthesis of precursor of [*N*-methyl- ^{11}C]vorozole, an efficient PET tracer targeting aromatase in the brain**

pp 1464–1470

Kayo Takahashi, Gen Yamagishi, Toshiyuki Hiramatsu, Ayako Hosoya, Kayo Onoe, Hisashi Doi, Hiroko Nagata, Yasuhiro Wada, Hirotaka Onoe, Yasuyoshi Watanabe, Takamitsu Hosoya*

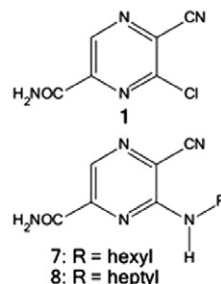


Synthesis and antimycobacterial properties of N-substituted 6-amino-5-cyanopyrazine-2-carboxamides

pp 1471–1476

Jan Zitko*, Martin Dolezal, Michaela Svobodova, Marcela Vejsova, Jiri Kunes, Radim Kucera, Petr Jilek

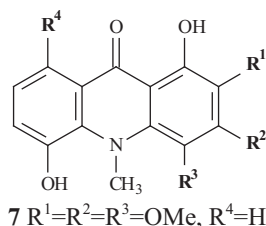
Antimycobacterial activity MIC [μg/mL]					
Compd.	<i>M. tuberculosis</i> H37Rv	<i>M. kansasii</i> 235/80	<i>M. avium</i> 80/72	<i>M. avium</i> 152/73	Clog P
1	25	25	25	25	-0.606
7	12.5	>200	>200	>200	2.297
8	12.5	100	100	100	2.826
PZA	12.5 - 25	>200	>200	>200	-0.676



Acridone alkaloids as potent inhibitors of cathepsin V

pp 1477–1481

Richele P. Severino, Rafael V. C. Guido, Emerson F. Marques, Dieter Brömme, M. Fátima das G. F. da Silva, João B. Fernandes, Adriano D. Andricopulo, Paulo C. Vieira*

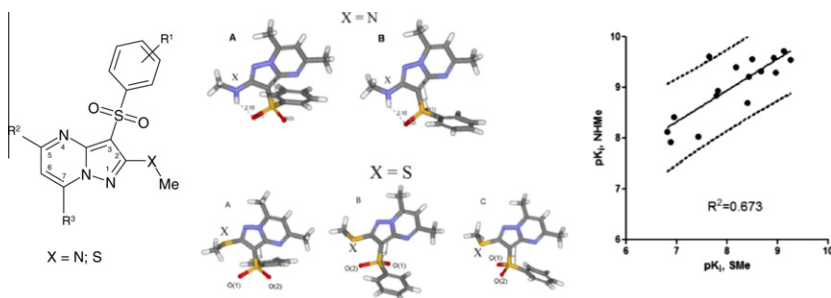


In this work, we describe the inhibitory effects of acridone alkaloids isolated from *Swinglea glutinosa* a plant belonging to the Rutaceae family. This class of compounds showed to be potent inhibitors of the enzyme cathepsin V. Some of the alkaloids displayed IC₅₀ values of inhibitory activity in the range of low μM. Mechanistic studies have clearly shown competitive inhibition with respect to substrate, with low dissociation constants: (**2**, K_i = 1.2 μM; **6**, K_i = 1.0 μM; **7**, K_i = 0.2 μM; and **11**, K_i = 1.7 μM).

Synthesis and SAR of 3-arylsulfonyl-pyrazolo[1,5-a]pyrimidines as potent serotonin 5-HT₆ receptor antagonists

pp 1482–1491

Alexandre V. Ivachtchenko, Elena S. Golovina, Madina G. Kadieva, Volodymyr M. Kysil, Oleg D. Mitkin, Sergey E. Tkachenko, Ilya Okun*

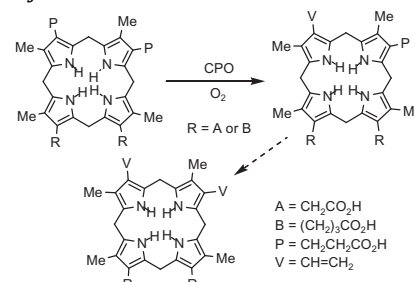


Normal and abnormal heme biosynthesis. Part 7. Synthesis and metabolism of coproporphyrinogen-III analogues with acetate or butyrate side chains on rings C and D. Development of a modified model for the active site of coproporphyrinogen oxidase

pp 1492–1504

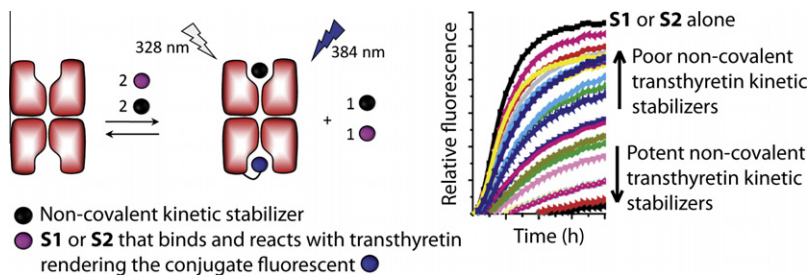
Timothy D. Lash*, Teresa R. Lamm, J. Andy Schaber, Wen-hsiang Chung, Eric K. Johnson, Marjorie A. Jones

Coproporphyrinogen analogues with acetate or butyrate groups in place of the usual propionate moieties on rings C and D have been used to probe the substrate binding requirements for coproporphyrinogen oxidase.



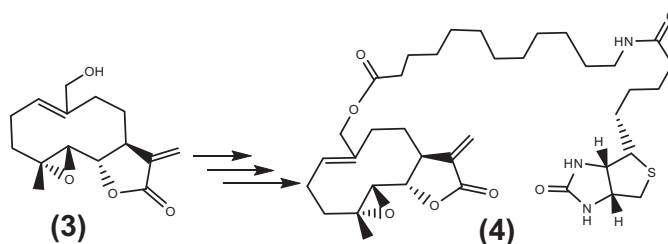
A competition assay to identify amyloidogenesis inhibitors by monitoring the fluorescence emitted by the covalent attachment of a stilbene derivative to transthyretin pp 1505–1514

Sungwook Choi, Jeffery W. Kelly*



Melampomagnolide B: A new antileukemic sesquiterpene pp 1515–1519

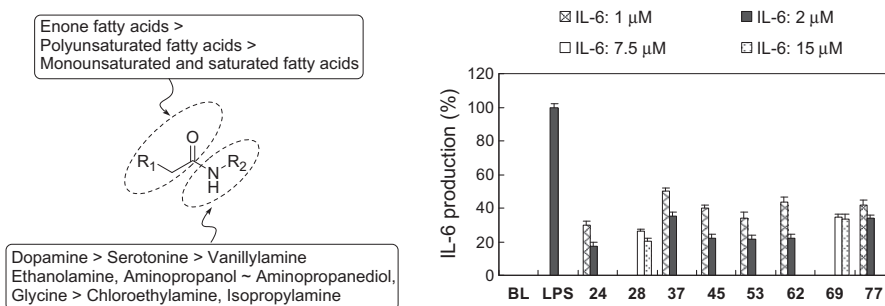
Shama Nasim, ShanShan Pei, Fred K. Hagen, Craig T. Jordan, Peter A Crooks*



Melampomagnolide B (3) has been identified as a new antileukemic sesquiterpene. A biotin-conjugated derivative (4) of melampomagnolide B was designed and synthesized in order to elucidate its mechanism of action. A study of the biochemical interactions of the biotin probe suggests that melampomagnolide B derives its remarkable selectivity for leukemic cells over normal hematopoietic cells from its unique ability to exploit biochemical differences between the two cell types.

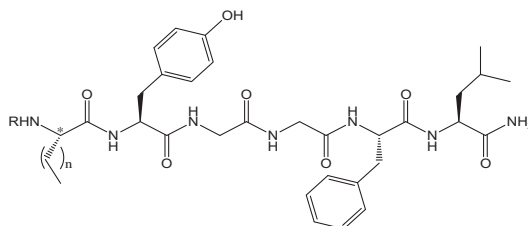
Evaluation of endogenous fatty acid amides and their synthetic analogues as potential anti-inflammatory leads pp 1520–1527

Hung The Dang, Gyeong Jin Kang, Eun Sook Yoo, Jongki Hong, Jae Sue Choi, Hyung Sik Kim, Hae Young Chung, Jee H. Jung*



Lipophilic derivatives of leu-enkephalinamide: In vitro permeability, stability and in vivo nasal delivery pp 1528–1534

Cécile D. Cros, Istvan Toth, Joanne T. Blanchfield*



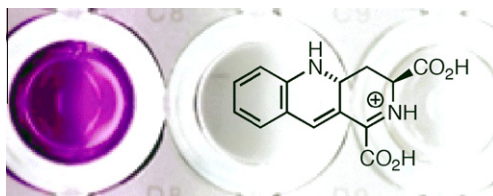
	R = H	R = CH ₃ CO
n = 5	C ₈ -Enk-NH ₂ (1)	Ac-C ₈ -Enk-NH ₂ (3)
n = 9	C ₁₂ -Enk-NH ₂ (2)	Ac-C ₁₂ -Enk-NH ₂ (4)



LC–MS and NMR characterization of the purple chromophore formed in the *o*-aminobenzaldehyde assay of dihydrodipicolinate synthase

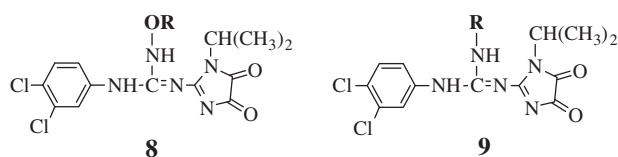
pp 1535–1540

Voula Mitsakos, Sean R. A. Devenish, Paul A. O'Donnell, Juliet A. Gerrard, Craig A. Hutton*

**New imidazolidinedione derivatives as antimalarial agents**

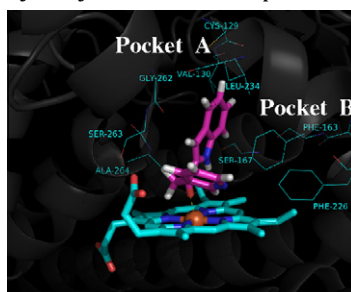
pp 1541–1549

Liang Zhang, Ramadas Sathunuru, ThuLan Luong, Victor Melendez, Michael P. Kozar, Ai J. Lin*

**R** = alkyl-, aryl-, alkylaryl-, aminoalkyl-**Indol-2-yl ethanones as novel indoleamine 2,3-dioxygenase (IDO) inhibitors**

pp 1550–1561

Eduard Dolušić, Pierre Larrieu, Sébastien Blanc, Frédéric Sapunarić, Bernadette Norberg, Laurence Moineaux, Delphine Colette, Vincent Stroobant, Luc Pilotte, Didier Colau, Thierry Ferain, Graeme Fraser, Moreno Galeni, Jean-Marie Frère, Bernard Masereel, Benoît Van den Eynde, Johan Wouters, Raphaël Frédérick*

**OTHER CONTENT****Corrigendum**

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Bioorganic & Medicinal Chemistry Reviews and Perspectives

pp I–III

*Corresponding author

Supplementary data available via ScienceDirect

COVER

Mutational activation of Ras GTPases is found in many types of cancers. The newly developed small molecule inhibitor, palmostatin B, inhibits depalmitoylation of Ras GTPases. This results in a loss of the proper localization of Ras GTPases and consequently their oncogenic signalling capacity is reduced. This provides a conceptually new approach for development of potential therapeutic agents that target oncogenic Ras signalling. The development of palmostatin B and its applications is summarized by Dekker and Hedberg in this issue. [Dekker, F. J.; Hedberg, C. *Bioorg. Med. Chem.* **2011**, 19, 1376–1380.]

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ISSN 0968-0896