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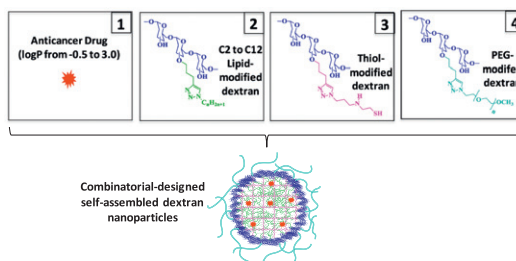
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'Click' synthesis of dextran macrostructures for combinatorial-designed self-assembled nanoparticles encapsulating diverse anticancer therapeutics

pp 6167–6173

Sampath C. Abeylath, Mansoor M. Amiji*

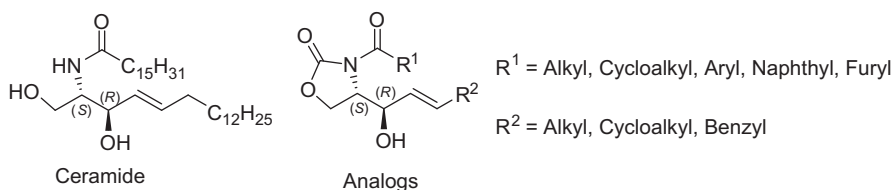


Schematic illustration for combinatorial approach in designing nanoparticle assemblies using C2 to C12 lipid-modified, thiol-modified, and poly(ethylene glycol) (PEG)-modified dextrans.

3,4-Disubstituted oxazolidin-2-ones as constrained ceramide analogs with anticancer activities

pp 6174–6181

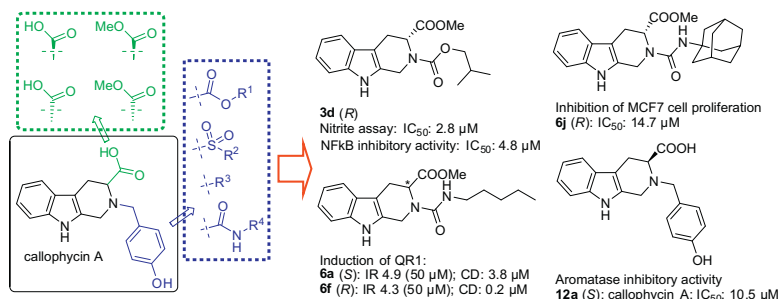
Alok Singh, Hyun-Joon Ha*, Jungchan Park, Jun Hee Kim, Won Koo Lee*



Design, synthesis, and biological evaluation of callophycin A and analogues as potential chemopreventive and anticancer agents

pp 6182–6195

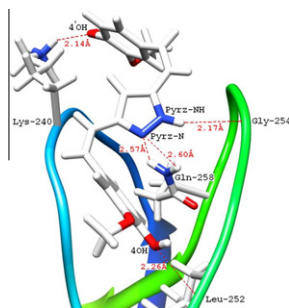
Li Shen, Eun-Jung Park, Tamara P. Kondratyuk, Daniela Guendisch, Laura Marler, John M. Pezzuto, Anthony D. Wright, Dianqing Sun*



Binding of isoxazole and pyrazole derivatives of curcumin with the activator binding domain of novel protein kinase C

pp 6196–6202

Joydip Das*, Satyabrata Pany, Shyam Panchal, Anjoy Majhi, Ghazi M. Rahman

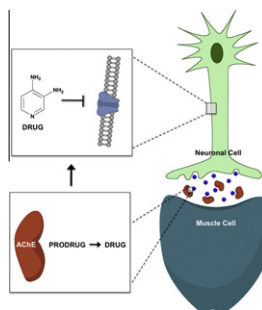


Binding of isoxazole and pyrazole derivatives of curcumin with PKC1B.

Formulating a new basis for the treatment against botulinum neurotoxin intoxication: 3,4-Diaminopyridine prodrug design and characterization

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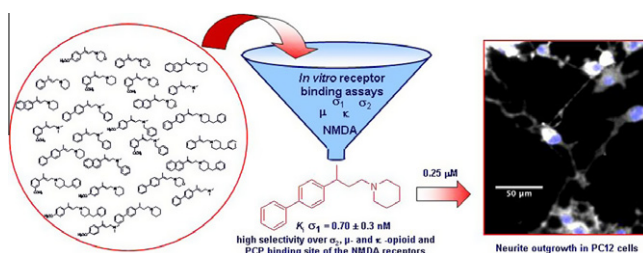
Joseph S. Zakhari, Isao Kinoyama, Mark S. Hixon, Antonia Di Mola, Daniel Globisch, Kim D. Janda*



Identification of a potent and selective σ_1 receptor agonist potentiating NGF-induced neurite outgrowth in PC12 cells

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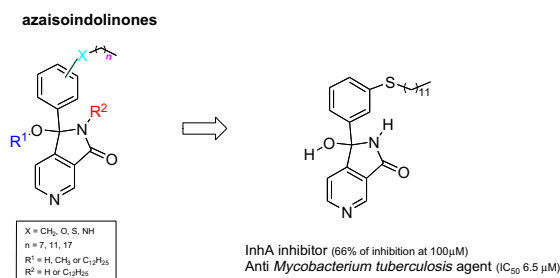
Daniela Rossi, Alice Pedrali, Mariangela Urbano, Raffaella Gaggeri, Massimo Serra, Leyden Fernández, Michael Fernández, Julio Caballero, Simone Ronsisvalle, Orazio Prezzavento, Dirk Schepmann, Bernhard Wuensch, Marco Peviani, Daniela Curti, Ornella Azzolina, Simona Collina*



Chemical synthesis, biological evaluation and structure–activity relationship analysis of azaisoindolinones, a novel class of direct enoyl-ACP reductase inhibitors as potential antimycobacterial agents

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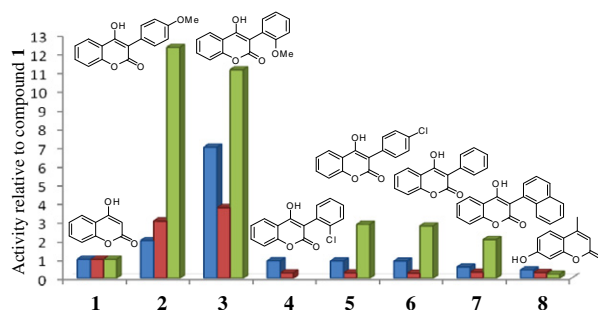
Céline Deraeve, Ioana Miruna Dorobantu, Farah Rebbah, Frédéric Le Quémener, Patricia Constant, Annaïk Quémard, Vania Bernardes-Génisson*, Jean Bernadou, Geneviève Pratviel



Effect of different C3-aryl substituents on the antioxidant activity of 4-hydroxycoumarin derivatives

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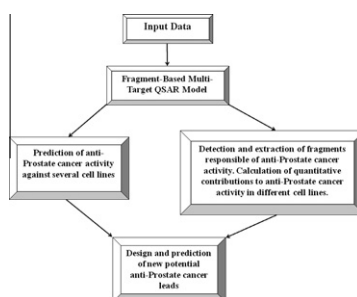
Sergio A. Rodríguez, Mónica A. Nazareno*, Maria T. Baumgartner*



Multi-target drug discovery in anti-cancer therapy: Fragment-based approach toward the design of potent and versatile anti-prostate cancer agents

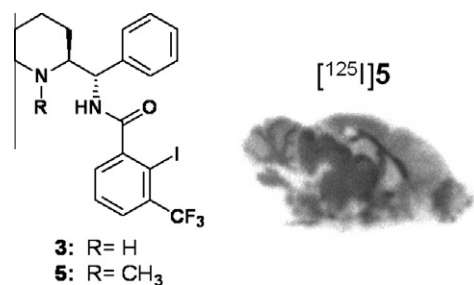
pp 6239–6244

Alejandro Speck-Planché*, Valeria V. Kleandrova, Feng Luan, M. Natália D. S. Cordeiro*

Synthesis and characterization of [¹²⁵I]2-iodo N-[(S)-((S)-1-methylpiperidin-2-yl)(phenyl)methyl]3-trifluoromethylbenzamide as novel imaging probe for glycine transporter 1

pp 6245–6253

Takeshi Fuchigami*, Mamoru Haratake, Yasuhiro Magata, Terushi Haradahira, Morio Nakayama*

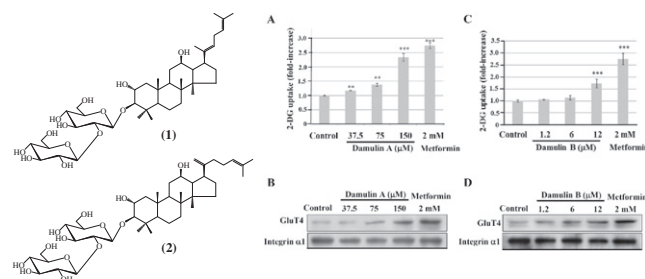


A series of radio-iodinated 1-methylpiperidin-2-yl benzamide derivatives have been synthesized and evaluated in vitro and in vivo as potential SPECT probes for imaging of glycine transporter 1.

New dammarane-type glucosides as potential activators of AMP-activated protein kinase (AMPK) from *Gynostemma pentaphyllum*

pp 6254–6260

Phi Hung Nguyen, Rehman Gauhar, Seung Lark Hwang, Trong Tuan Dao, Dong Chan Park, Ji Eun Kim, Hebok Song, Tae Lin Huh*, Won Keun Oh*



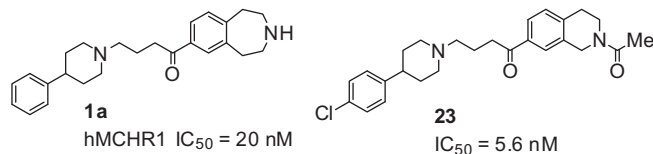
Two novel dammarane-type saponins, damulins A (1) and B (2), that strongly activate AMPK in cultured L6 myotube cells was isolated from *Gynostemma pentaphyllum*. Damulins A and B also increased β -oxidation and glucose uptake with increasing GluT4 translocation to the plasma membrane in L6 myotube cells. These results indicate that activation of AMPK by damulins A and B may contribute to beneficial effect of *G. pentaphyllum* on glucose and lipid metabolism.



Melanin-concentrating hormone receptor 1 antagonists: Synthesis, structure–activity relationship, docking studies, and biological evaluation of 2,3,4,5-tetrahydro-1H-3-benzazepine derivatives

pp 6261–6273

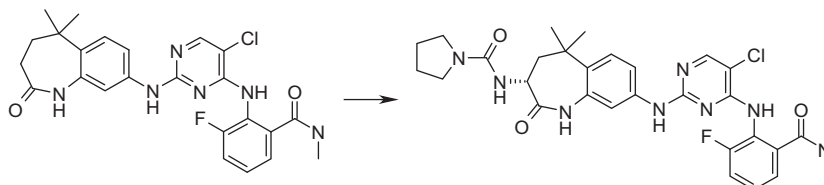
Shizuo Kasai*, Masahiro Kamaura, Makoto Kamata, Kazuyoshi Aso, Hitomi Ogino, Yoshihide Nakano, Kaoru Watanabe, Tomoko Kaisho, Michiko Tawada, Yasutaka Nagisa, Shiro Takekawa, Koki Kato, Nobuhiro Suzuki, Yuji Ishihara



Improvement in oral bioavailability of 2,4-diaminopyrimidine c-Met inhibitors by incorporation of a 3-amidobenzazepin-2-one group

pp 6274–6284

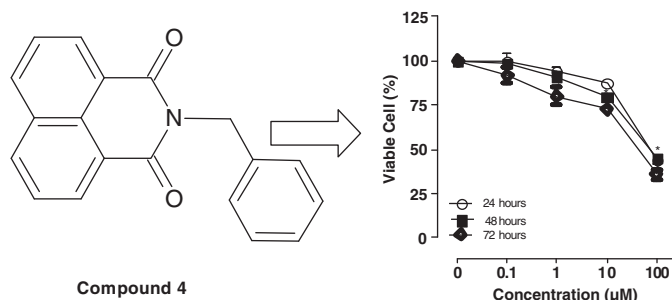
Karen L. Milkiewicz*, Lisa D. Aimone, Mark S. Albom, Thelma S. Angeles, Hong Chang, Jennifer V. Grobelny, Jean Husten, Christine LoSardo, Sheila Miknyoczki, Seetha Murthy, Damaris Rolon-Steele, Ted L. Underiner, Linda R. Weinberg, Candace S. Worrell, Kelli S. Zeigler, Bruce D. Dorsey



Evaluation of apoptotic effect of cyclic imide derivatives on murine B16F10 melanoma cells

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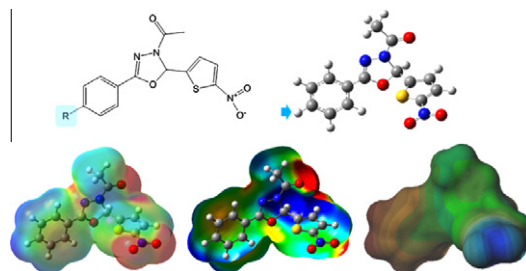
Karina Elisa Machado, Kely Navakoski de Oliveira, Lorena Santos-Bubniak, Marley Aparecida Licínio, Ricardo José Nunes, Maria Cláudia Santos-Silva*



Synthesis, molecular modeling and preliminary biological evaluation of a set of 3-acetyl-2,5-disubstituted-2,3-dihydro-1,3,4-oxadiazole as potential antibacterial, anti-*Trypanosoma cruzi* and antifungal agents

pp 6292–6301

Marina Ishii*, Salomão Dória Jorge, Alex Alfredo de Oliveira, Fanny Palace-Berl, Ieda Yuriko Sonehara, Kerly Fernanda Mesquita Pasqualoto, Leoberto Costa Tavares

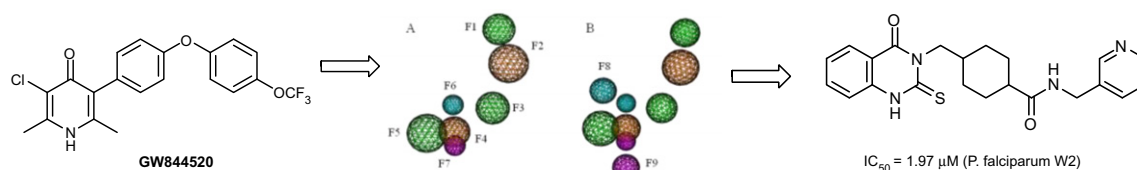


A novel set of 3-acetyl-2,5-disubstituted-2,3-dihydro-1,3,4-oxadiazole has been synthesized and its antiprotozoal, antibacterial and antifungal activities evaluated. Also, their physicochemical and structural properties were explored to establish qualitative property–activity relationships.

Identification of new antimalarial leads by use of virtual screening against cytochrome bc₁

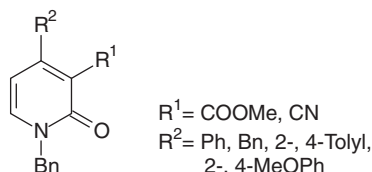
pp 6302–6308

Tiago Rodrigues, Rui Moreira*, Jiri Gut, Philip J. Rosenthal, Paul M. O'Neill, Giancarlo A. Biagini, Francisca Lopes, Daniel J.V. A. dos Santos, Rita C. Guedes

**Discovery of pyridine-2-ones as novel class of multidrug resistance (MDR) modulators: First structure–activity relationships**

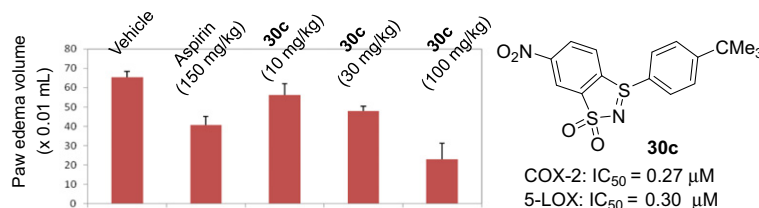
pp 6309–6315

Sören Krawczyk, Monika Otto, Alexander Otto, Claudius Coburger, Martin Krug, Marianne Seifert, Volkmar Tell, József Molnár, Andreas Hilgeroth*

**Design, synthesis and biological evaluation of benzo[1.3.2]dithiazolium ylide 1,1-dioxide derivatives as potential dual cyclooxygenase-2/5-lipoxygenase inhibitors**

pp 6316–6328

Chen-Ming Tan, Grace Shiahuy Chen, Chien-Shu Chen, Pei-Teh Chang, Ji-Wang Chern*

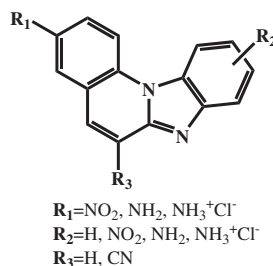


The structure–activity relationship of a series of benzo[1.3.2]dithiazolium ylide 1,1-dioxide derivatives was studied. 6-Nitro group was crucial for dual COX-2/5-LOX inhibitory activity. The most potent compound **30c** exhibited anti-inflammatory activity in the carrageenan-induced paw edema assay in male Wistar rats.

Novel biologically active nitro and amino substituted benzimidazo[1,2-a]quinolines

pp 6329–6339

Nataša Perin, Lidija Uzelac, Ivo Piantanida, Grace Karminski-Zamola, Marijeta Kralj*, Marijana Hranjec*



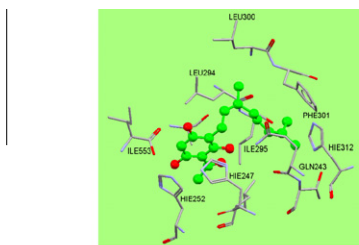
Novel benzimidazo[1,2-a]quinolines showed significant growth inhibitory effect towards five tumor cell lines (IC₅₀ = 2–19 μM). Fluorescence microscopy study showed cytoplasmic distribution of the compounds, demonstrating that DNA is not the primary target of compounds.



Bioassay-guided identification of an anti-inflammatory prenylated acylphloroglucinol from *Melicope ptelefolia* and molecular insights into its interaction with 5-lipoxygenase

pp 6340–6347

Khozirah Shaari*, Velan Suppaiah, Lam Kok Wai, Johnson Stanslas, Bimo Ario Tejo, Daud Ahmad Israf, Faridah Abas, Intan Safinar Ismail, Nor Hasifi Shuaib, Seema Zareen, Nordin Hj. Lajis



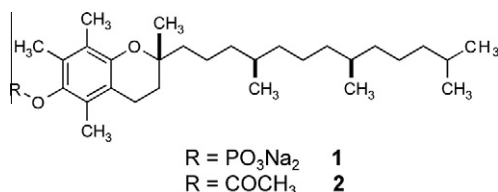
Inhibition on 5-LOX activity by thGA (IC₅₀ = 0.42 μM)



Sodium di- α -tocopheryl-6-O-phosphate inhibits PGE₂ production in keratinocytes induced by UVB, IL-1 β and peroxidants

pp 6348–6355

Eiko Kato, Yuichi Sasaki, Noriko Takahashi*

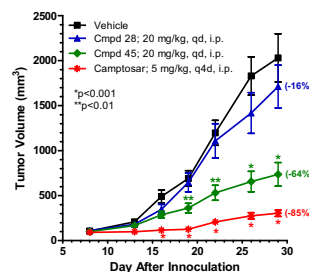
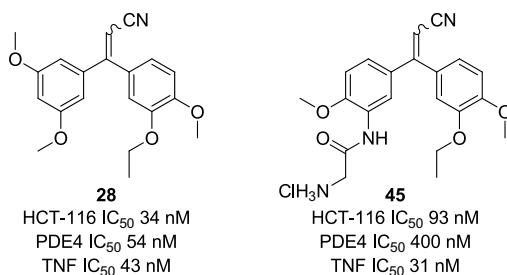


Compound **1** is an excellent inhibitor of inflammatory mediators and serves as a protective agent against exogenous stimulants.

1,1-Diaryllalkenes as anticancer agents: Dual inhibitors of tubulin polymerization and phosphodiesterase 4

pp 6356–6374

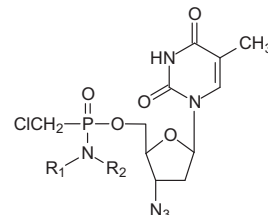
Alexander L. Ruchelman*, Hon-Wah Man, Roger Chen, Wei Liu, Ling Lu, Dorota Cedzik, Ling Zhang, Jim Leisten, Alice Collette, Rama Krishna Narla, Heather K. Raymon, George W. Muller



Synthesis and anticancer activity of 5'-chloromethylphosphonates of 3'-azido-3'-deoxythymidine (AZT)

pp 6375–6382

Lech Celewicz*, Agnieszka Jóźwiak, Piotr Ruszkowski, Halina Laskowska, Anna Olejnik, Anna Czarnecka, Marcin Hoffmann, Bogusław Hładoń



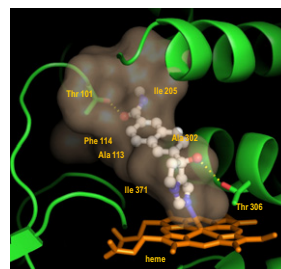
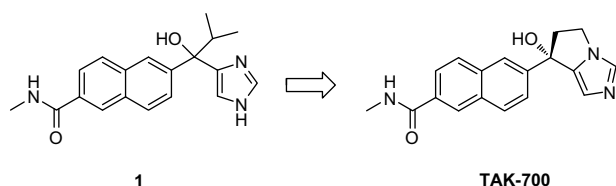
10 examples
the most active compound (R₁ = H, R₂ = n-Pr)
IC₅₀ = 3.7 μg/mL (MCF-7)

A series of novel N-alkyl 5'-chloromethylphosphonates of 3'-azido-3'-deoxythymidine (AZT) were synthesized and evaluated for their cytotoxic activity in two human cancer cell lines: oral (KB) and breast (MCF-7).

Discovery of orteronel (TAK-700), a naphthylmethylimidazole derivative, as a highly selective 17,20-lyase inhibitor with potential utility in the treatment of prostate cancer

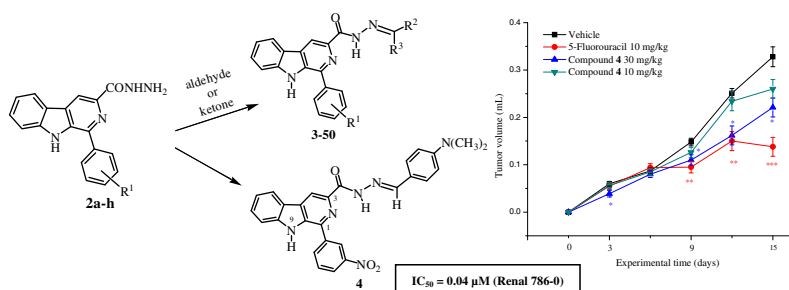
pp 6383–6399

Tomohiro Kaku*, Takenori Hitaka, Akio Ojida, Nobuyuki Matsunaga, Mari Adachi, Toshimasa Tanaka, Takahito Hara, Masuo Yamaoka, Masami Kusaka, Teruaki Okuda, Satoru Asahi, Shuichi Furuya, Akihiro Tasaka

**Synthesis and antitumor activity of β -carboline 3-(substituted-carbohydrazide) derivatives**

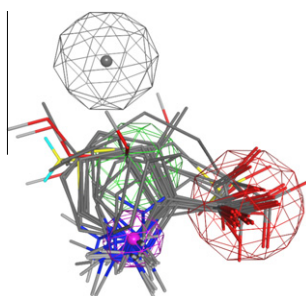
pp 6400–6408

Valéria Aquilino Barbosa, Anelise S. Nazari Formagio, Franciele Cristina Savariz, Mary Ann Foglio, Humberto Moreira Spindola, João Ernesto de Carvalho, Emerson Meyer, Maria Helena Sarrajiotto*

**Three-dimensional quantitative structure–activity relationship analyses of substrates of the human proton-coupled amino acid transporter 1 (hPAT1)**

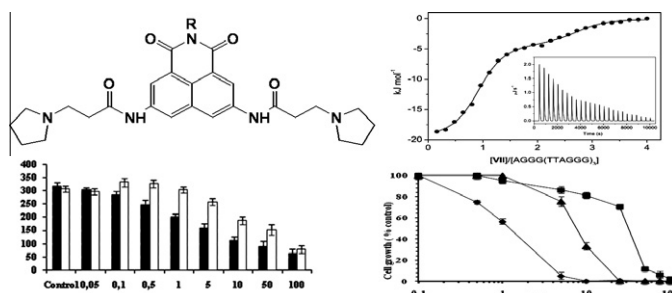
pp 6409–6418

Iris Thondorf*, Valerie Voigt, Sarah Schäfer, Sabine Gebauer, Katja Zebisch, Linda Laug, Matthias Brandsch

**Design, synthesis, biophysical and biological studies of trisubstituted naphthalimides as G-quadruplex ligands**

pp 6419–6429

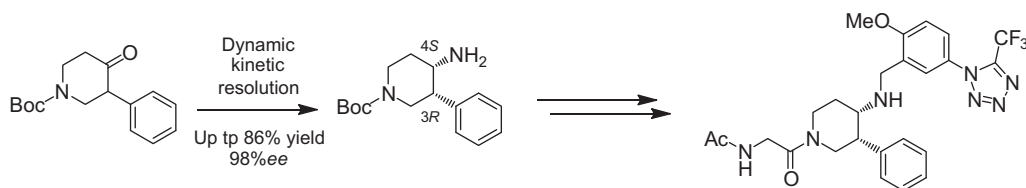
Antonella Peduto, Bruno Pagano, Carmen Petronzi, Antonio Massa, Veronica Esposito, Antonella Virgilio, Francesco Paduano, Francesco Trapasso, Filomena Fiorito, Salvatore Florio, Concetta Giancola, Aldo Galeone*, Rosanna Filosa*



Design, structure–activity relationship, and highly efficient asymmetric synthesis of 3-phenyl-4-benzylaminopiperidine derivatives as novel neurokinin-1 receptor antagonists

pp 6430–6446

Junya Shirai*, Takeshi Yoshikawa, Masayuki Yamashita, Yasuharu Yamamoto, Makiko Kawamoto, Naoki Tarui, Izumi Kamo, Tadatashi Hashimoto, Yoshinori Ikeura

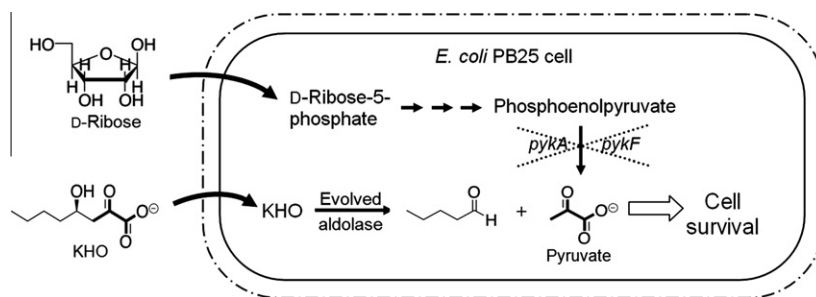


A series of novel and potent 3-phenyl-4-benzylaminopiperidine tachykinin NK₁ antagonists are described. Highly efficient asymmetric synthesis of this series is achieved via dynamic kinetic resolution.

Directed evolution of a pyruvate aldolase to recognize a long chain acyl substrate

pp 6447–6453

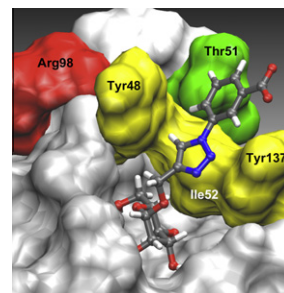
Manoj Cheriyan, Matthew J. Walters, Brian D. Kang, Laura L. Anzaldi, Eric J. Toone, Carol A. Fierke*



Design, synthesis and biological evaluation of mannosyl triazoles as FimH antagonists

pp 6454–6473

Oliver Schwardt, Said Rabbani, Margrit Hartmann, Daniela Abgottspon, Matthias Wittwer, Simon Kleeb, Adam Zalewski, Martin Smieško, Brian Cutting, Beat Ernst*



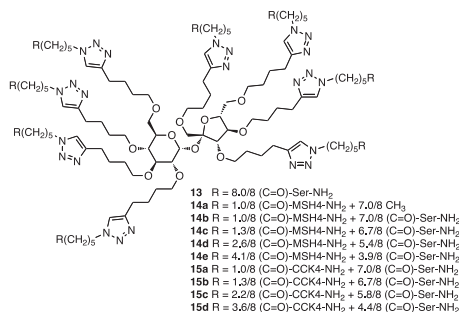
X-ray structures of FimH co-crystallized with two different ligands, the physiological binding epitope oligomannose-3 and a biphenyl α -D-mannoside revealed different binding modes, an *in-docking-mode* and an *out-docking-mode*, respectively. To accomplish the *in-docking-mode*, that is the docking mode where the ligand is hosted by the so-called tyrosine gate, FimH antagonists with increased flexibility were designed, synthesized and evaluated.



A sucrose-derived scaffold for multimerization of bioactive peptides

pp 6474–6482

Venkataramanarao Rao, Ramesh Alleti, Liping Xu, Narges K. Tafreshi, David L. Morse, Robert J. Gillies, Eugene A. Mash*



pp 6483–6491

[illegible]

pp 6492–6504

$$(\text{CH}_2\text{O})_x + \begin{array}{c} \text{R}^1 \\ | \\ \text{NH} \\ | \\ \text{R}^2 \end{array} + \text{R}^3\text{—NC} + \text{TMSN}_3 \longrightarrow \begin{array}{c} \text{R}^1 \\ | \\ \text{N} \text{---} \text{CH}_2 \text{---} \text{N} \\ | \quad \quad | \\ \text{R}^2 \quad \quad \text{R}^3 \end{array} \longrightarrow \begin{array}{c} \text{R}^1 \\ | \\ \text{N} \text{---} \text{CH}_2 \text{---} \text{N} \\ | \quad \quad | \\ \text{R}^2 \quad \quad \text{N} \text{---} \text{N} \text{---} \text{N} \end{array}$$


pp 6505–6517

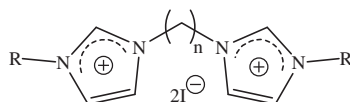
The figure shows the chemical structures of two macrocyclic compounds, 1 and 2, and their retrosynthetic analysis. Structure 1 is a 21-membered ring macrocycle with a 4-phenyl-4-hydroxybutyl side chain. Structure 2 is a 23-membered ring macrocycle with a 4-phenyl-4-hydroxybutyl side chain. Both structures are complex polycyclic molecules containing multiple amide and ester linkages. A retrosynthetic arrow labeled "RCM mimic" points from structure 1 to structure 2, indicating that structure 2 is a macrocyclic mimic of structure 1, where the side chain has been incorporated into the macrocycle.



pp 6518–6524

The anti-malarial activity of bivalent imidazolium salts**pp 6525–6542**

Jason Z. Vlahakis, Simona Mitu, Gheorghe Roman, E. Patricia Rodriguez, Ian E. Crandall*, Walter A. Szarek*

**Bis-imidazolium salts**

R = alkyl

n = 2, 4, 6, 8, 10–16, 18, 20

Novel bis-imidazolium salts have been synthesized and showed highly potent and selective anti-*Plasmodium* activity.

*Corresponding author

* Supplementary data available via SciVerse ScienceDirect

COVER

The known veterinary anthelmintic and proton ionophore, closantel, was recently discovered to also exhibit potent chitinase inhibition activity and inhibit molting in the parasitic nematode, *Onchocerca volvulus*, the causative agent of the neglected tropical disease onchocerciasis. [C. Gloeckner, A. L. Garner, F. Mersha, Y. Oksov, N. Tricoche, L. M. Eubanks, S. Lustigman, G. F. Kaufmann, K. D. Janda, Repositioning of an existing drug for the neglected tropical disease Onchocerciasis, *Proc. Natl. Acad. Sci., U.S.A.* **2010**, 107, 3424.]

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