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# Bioorganic & Medicinal Chemistry

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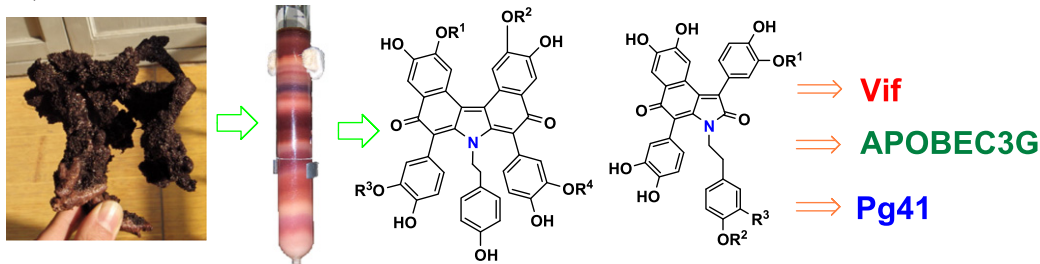
## Bioorganic & Medicinal Chemistry Volume 18, Issue 15, 2010

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#### ARTICLES

- Baculiferins A–O, O-sulfated pyrrole alkaloids with anti-HIV-1 activity, from the Chinese marine sponge *Iotrochota baculifera*** pp 5466–5474

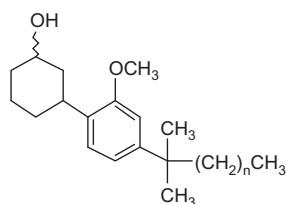
Guotao Fan, Zelin Li\*, Shi Shen, Yi Zeng, Yishu Yang, Minjuang Xu, Torsten Bruhn, Heike Bruhn, Joachim Morschhäuser, Gerhard Bringmann\*, Wenhan Lin\*



- Synthesis and pharmacology of 1-methoxy analogs of CP-47,497**

pp 5475–5482

John W. Huffman\*, Seon A. Hepburn, Patricia H. Reggio, Dow P. Hurst, Jenny L. Wiley, Billy R. Martin

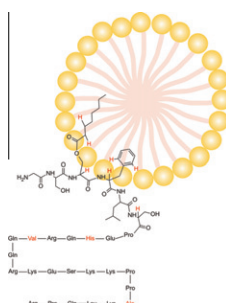


The synthesis and pharmacology of three 1-methoxy analogs of CP-47,497 ( $n = 4$  and  $5$ ) are described. The CB<sub>1</sub> and CB<sub>2</sub> receptor affinities of these compounds are reported. Molecular modeling and receptor docking studies are presented.

- The peptide hormone ghrelin binds to membrane-mimetics via its octanoyl chain and an adjacent phenylalanine**

pp 5483–5488

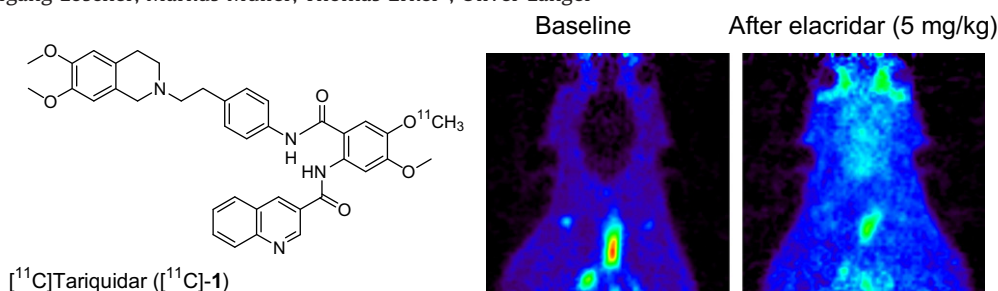
Jörg Großauer, Simone Kosol, Evelyne Schrank, Klaus Zangger\*



### Synthesis and in vivo evaluation of [ $^{11}\text{C}$ ]tariquidar, a positron emission tomography radiotracer based on a third-generation P-glycoprotein inhibitor

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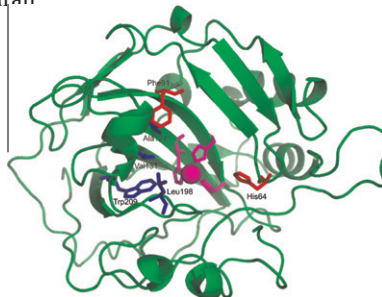
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### Mutation of Phe91 to Asn in human carbonic anhydrase I unexpectedly enhanced both catalytic activity and affinity for sulfonamide inhibitors

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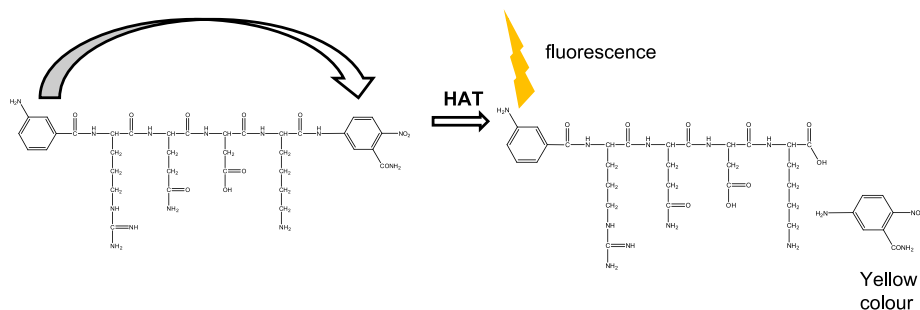
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### Substrate specificity and inhibitory study of human airway trypsin-like protease

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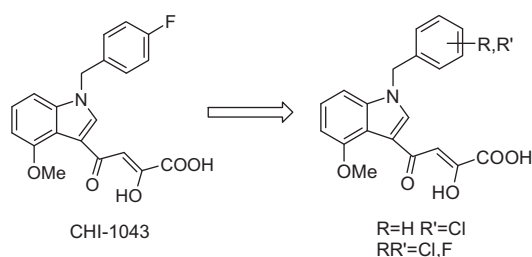
M. Wysocka, B. Spichalska, A. Lesner\*, M. Jaros, K. Brzozowski, A. Łęgowska, K. Rolka



### New chloro,fluorobenzylindole derivatives as integrase strand-transfer inhibitors (INSTIs) and their mode of action

pp 5510–5518

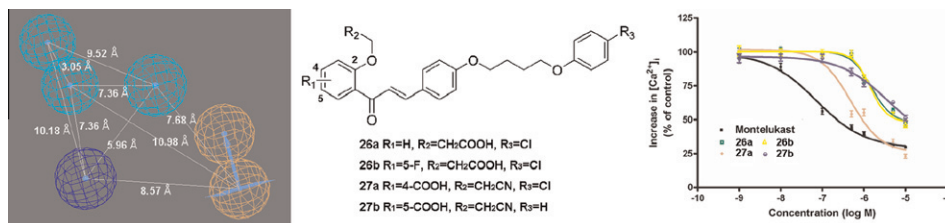
Stefania Ferro, Laura De Luca\*, Maria Letizia Barreca, Sara De Grazia, Frauke Christ, Zeger Debyser, Alba Chimirri



## Pharmacophore identification, synthesis, and biological evaluation of carboxylated chalcone derivatives as CysLT<sub>1</sub> antagonists

pp 5519–5527

Xiaowu Dong, Li Wang, Xueqin Huang, Tao Liu, Erqing Wei, Lilin Du, Bo Yang, Yongzhou Hu\*



The pharmacophore model (Hypo1) for CysLT<sub>1</sub> antagonists was developed. Virtual screening against an in-house database using Hypo1 was performed. Retrieved hits **26a,b** and **27a,b** were synthesized and biological evaluated for their CysLT<sub>1</sub> antagonistic activities.

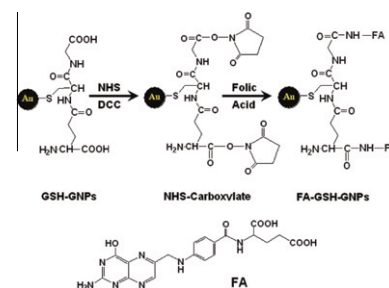


## Conjugating folic acid to gold nanoparticles through glutathione for targeting and detecting cancer cells

pp 5528–5534

Zhaowu Zhang, Jing Jia, Youqun Lai, Yanyan Ma, Jian Weng, Liping Sun\*

Folic acid-functionalized gold nanoparticles were prepared by a three-step approach. The thiol group of glutathione conjugates with gold nanoparticles through Au–S bond. DCC and NHS are used to activate the carboxyl groups of GSH, forming a highly reactive intermediate. The activated carboxyl groups react subsequently with the free amino group presented in folic acid, resulting in the formation of folic acid-conjugated nanoparticles.

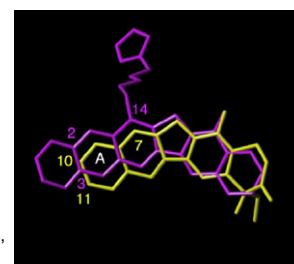
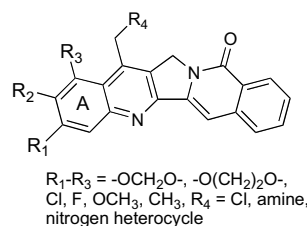


## The structure–activity relationships of A-ring-substituted aromathecine topoisomerase I inhibitors strongly support a camptothecin-like binding mode

pp 5535–5552

Maris A. Cinelli, Andrew E. Morrell, Thomas S. Dexheimer, Keli Agama, Surbhi Agrawal, Yves Pommier, Mark Cushman\*

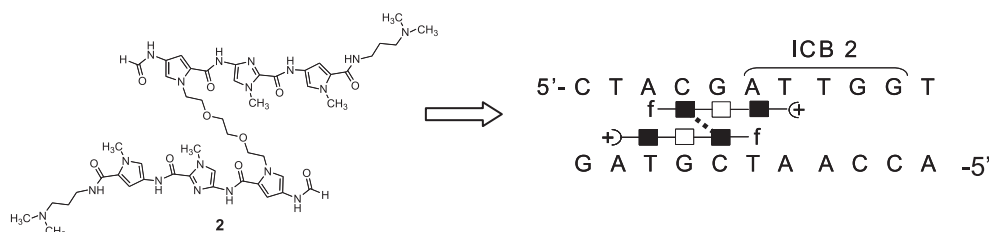
Novel aromathecines, substituted at four different positions, were prepared and evaluated against Top1 and human tumor cells. SAR trends mimic those of camptothecin and support our proposed camptothecin-like binding mode.



## Targeting the ICB2 site of the topoisomerase II $\alpha$ promoter with a formamido-pyrrole-imidazole-pyrrole H-pin polyamide

pp 5553–5561

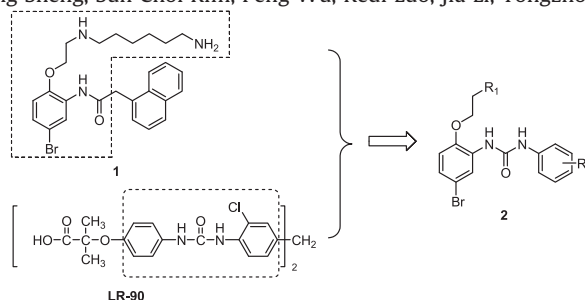
Andrew Franks, Christopher Tronrud, Konstantinos Kiakos, Jerome Kluza, Manoj Munde, Toni Brown, Hilary Mackay, W. David Wilson, Daniel Hochhauser, John A. Hartley, Moses Lee\*





**Dual-target-directed 1,3-diphenylurea derivatives: BACE 1 inhibitor and metal chelator against Alzheimer's disease** pp 5610–5615

Wenhai Huang, Dan Lv, Haiping Yu, Rong Sheng, Sun Chol Kim, Peng Wu, Kedi Luo, Jia Li, Yongzhou Hu\*

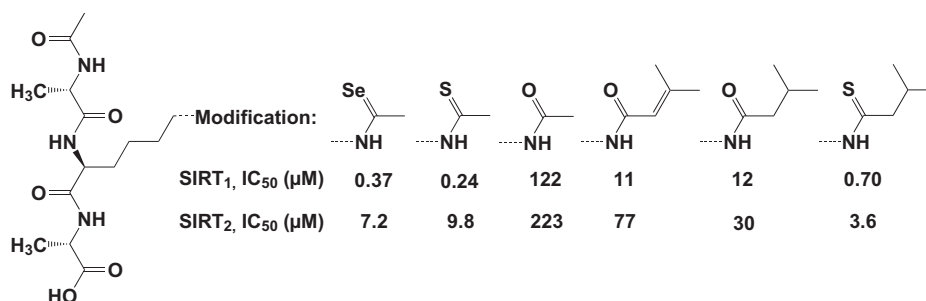


Dual-target-directed 1,3-diphenylurea derivatives were designed by hybridizing BACE 1 inhibitor **1** with metal chelator LR-90. Eleven compounds with favorable Fitvalues were selected, synthesized and evaluated for their BACE 1 inhibitory activities and the ability to function as metal chelators.

**N<sup>ε</sup>-Modified lysine containing inhibitors for SIRT1 and SIRT2**

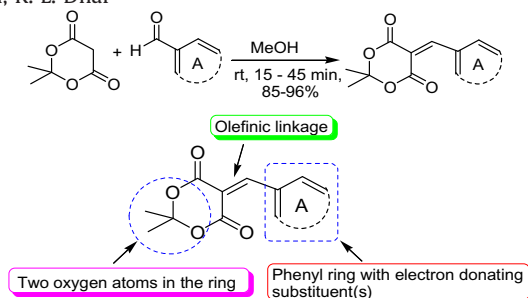
pp 5616–5625

Tero Huhtiniemi\*, Tiina Suuronen, Maija Lahtela-Kakkonen, Tanja Bruijn, Sanna Jääskeläinen, Antti Poso, Antero Salminen, Jukka Leppänen, Elina Jarho

**Synthesis and biological evaluation of arylidene analogues of Meldrum's acid as a new class of antimalarial and antioxidant agents**

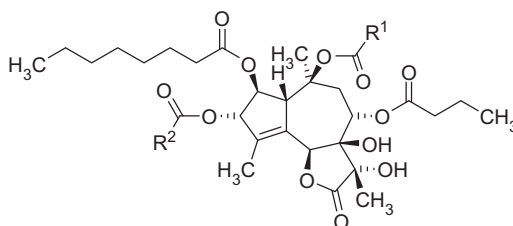
pp 5626–5633

Harmeet S. Sandhu, Sameer Sapra, Mukesh Gupta, Kunal Nepali, Raju Gautam, Sunil Yadav, Raj Kumar\*, Sanjay M. Jachak, Manoj Chugh, Manish K. Gupta, Om P. Suri, K. L. Dhar

**Elucidation of the topography of the thapsigargin binding site in the sarco-endoplasmic calcium ATPase**

pp 5634–5646

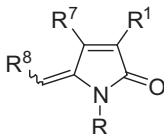
Dorthe Mondrup Skytte, Jesper Vuust Møller, Huizhen Liu, Helle Østergren Nielsen, Louise Elsa Svenningsen, Christina Mernøe Jensen, Carl Erik Olsen, Søren Brøgger Christensen\*



### Synthesis, binding and bioactivity of $\gamma$ -methylene $\gamma$ -lactam ecdysone receptor ligands: Advantages of QSAR models for flexible receptors

pp 5647–5660

Woldeamanuel Birru, Ross T. Fernley, Lloyd D. Graham, Julian Grusovin, Ronald J. Hill, Albert Hofmann, Linda Howell, Peter J. James, Karen E. Jarvis, Wynona M. Johnson, Dionne A. Jones, Christa Leitner, Andris J. Liepa, George O. Lovrecz, Louis Lu, Roland H. Nearn, Brian J. O'Driscoll, Tram Phan, Matthew Pollard, Kathleen A. Turner\*, David A. Winkler\*



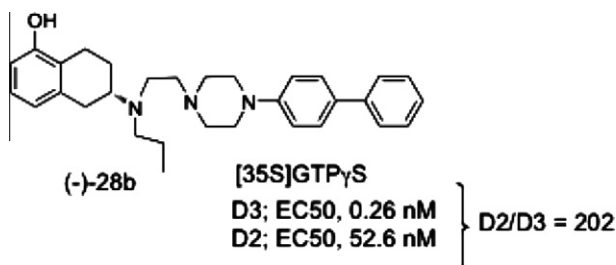
Probing adaptable receptors: a new class of ligand for the ecdysone receptor demonstrates the utility of QSAR for investigating binding site shapes in conformationally plastic nuclear hormone receptors.



### Further delineation of hydrophobic binding sites in dopamine D<sub>2</sub>/D<sub>3</sub> receptors for *N*-4 substituents on the piperazine ring of the hybrid template 5/7-[[2-(4-aryl-piperazin-1-yl)-ethyl]-propyl-amino]-5,6,7,8-tetrahydro-naphthalen-2-ol

pp 5661–5674

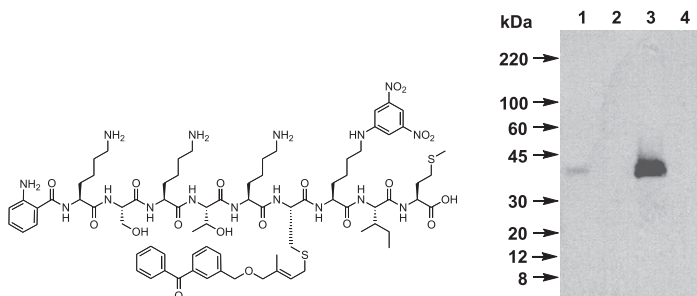
Balaram Ghosh, Tamara Antonio, Bhaskar Gopishetty, Maarten Reith, Alope Dutta\*



### Photoaffinity labeling of Ras converting enzyme 1 (Rce1p) using a benzophenone-containing peptide substrate

pp 5675–5684

Kelly Kyro, Surya P. Manandhar, Daniel Mullen, Walter K. Schmidt, Mark D. Distefano\*

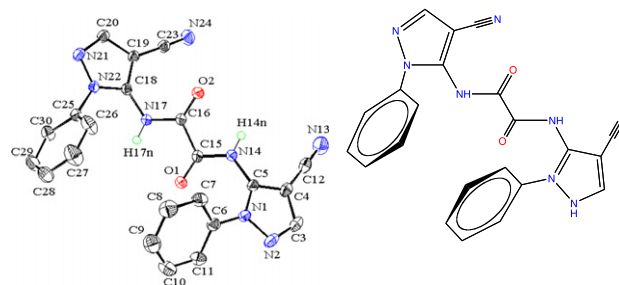


### Synthesis and biological evaluation of novel pyrazole compounds

pp 5685–5696

Amal M. Youssef, Edward G. Neeland, Erika B. Villanueva, M. Sydney White, Ibrahim M. El-Ashmawy, Brian Patrick, Andis Klegeris\*, Alaa S. Abd-El-Aziz\*

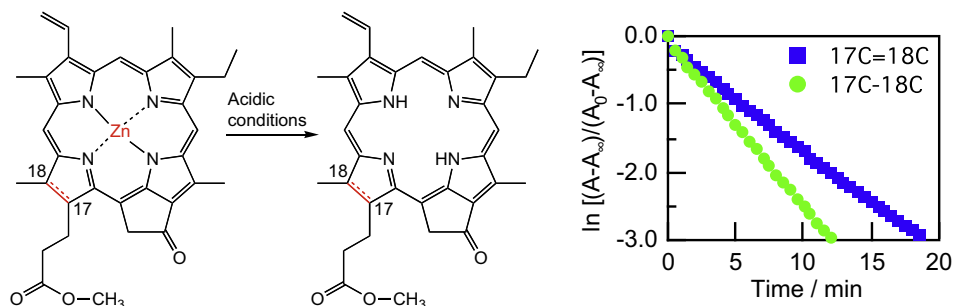
A novel dipyrazole ethandiamide lead compound **3** has been synthesized and reacted with a number of nucleophiles. Two compounds (**3** and **4d**) were identified as novel neuroprotective and anti-inflammatory agents within this study.



**Comparison of demetalation properties between zinc chlorin and zinc porphyrin derivatives: Effect of macrocyclic structures**

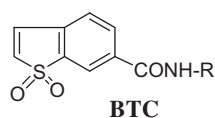
pp 5697–5700

Yoshitaka Saga\*, Sayaka Hojo, Yuki Hirai

**Benzo[b]thiophene-6-carboxamide 1,1-dioxides: Inhibitors of human cancer cell growth at nanomolar concentrations**

pp 5701–5707

Aitziber A. Sagardoy, María J. Gil, Raquel Villar, María J. Viñas, Aranzazu Arrazola, Ignacio Encío, Victor Martinez-Merino\*

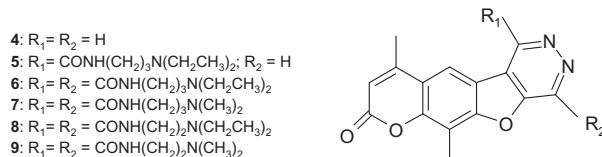


New BTC showed nM GI<sub>50</sub> against HTB-54, CCRF-CEM and HeLa and sub-μM against K-562, MEL-AC and HT-29 tumour cell lines. BTC induced apoptosis in CCRF-CEM and a significant increase in the rate of intracellular ROS generation.

**Pyridazinopsoralens of wide chemotherapeutic interest**

pp 5708–5714

Lisa Dalla Via\*, Ornella Gia, Sebastiano Marciani Magno, Alessandra Braga, José Carlos González-Gómez, Lázaro Guillermo Pérez-Montoto, Eugenio Uriarte

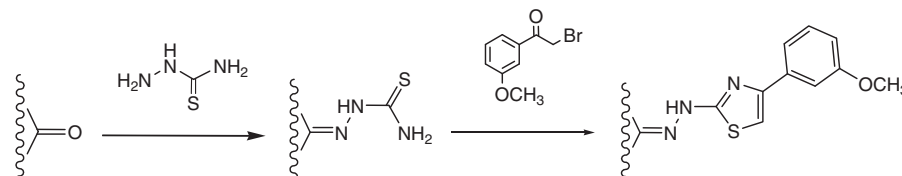


The synthesis of 6,10-dimethylpyridazino[4,5-*h*]psoralen derivatives is described. The new compounds demonstrate both a UVA-dependent and independent antiproliferative activity, intercalate into DNA and behave as topoisomerase II catalytic inhibitors.

**Investigations on the 2-thiazolylhydrazine scaffold: Synthesis and molecular modeling of selective human monoamine oxidase inhibitors**

pp 5715–5723

Franco Chimenti, Adriana Bolasco\*, Daniela Secci, Paola Chimenti, Arianna Granese, Simone Carradori, Matilde Yáñez, Francisco Orallo, Francesco Ortuso, Stefano Alcaro

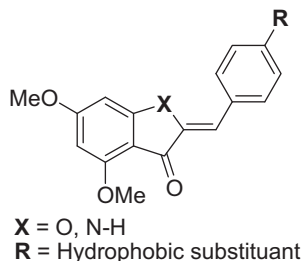




### 1-Azaaurones derived from the naturally occurring aurones as potential antimalarial drugs

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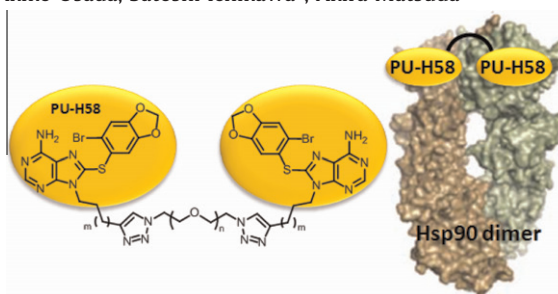
Florence Souard\*, Sabrina Okombi, Chantal Beney, Séverine Chevalley, Alexis Valentin, Ahcène Boumendjel



### Efficient synthesis of Hsp90 inhibitor dimers as potential antitumor agents

pp 5732–5737

Hironori Sekiguchi, Kazuhiro Muranaka, Akiko Osada, Satoshi Ichikawa\*, Akira Matsuda\*

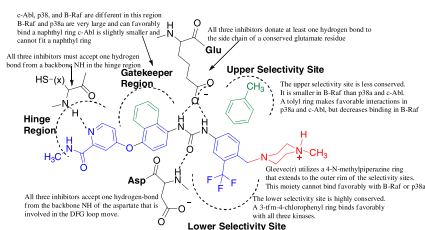


The PU-H58-dimers were designed as potential Hsp90 inhibitors and efficiently synthesized by the copper-catalyzed alkyne azide coupling (CuAAC) and their biological properties including binding affinity to the N-terminal domain of Hsp90, cytotoxicity, and client degradation activity were evaluated.

### The design, synthesis, and evaluation of 8 hybrid DFG-out allosteric kinase inhibitors: A structural analysis of the binding interactions of Gleevec®, Nexavar®, and BIRB-796

pp 5738–5748

Justin Dietrich\*, Christopher Hulme, Laurence H. Hurley

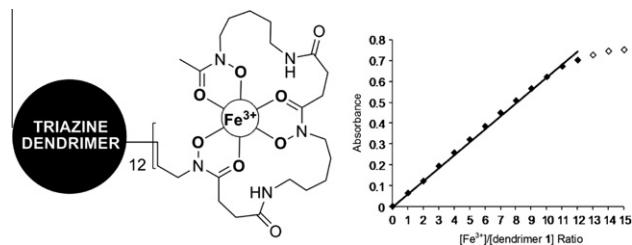


Here, we present a structural comparison of the important and similar interactions necessary for Gleevec®, Nexavar®, and BIRB-796 to bind to their respective DFG-out allosteric binding pockets and the selectivity of each with respect to c-Abl, B-Raf, and p38 $\alpha$ . A structural analysis of their selectivity profiles has been generated from the synthesis and evaluation of eight additional DFG-out allosteric inhibitors that were developed directly from fragments of these successful scaffolds.

### Synthesis and characterization of a triazine dendrimer that sequesters iron(III) using 12 desferrioxamine B groups

pp 5749–5753

Jongdoo Lim, Vincent J. Venditto, Eric E. Simanek\*



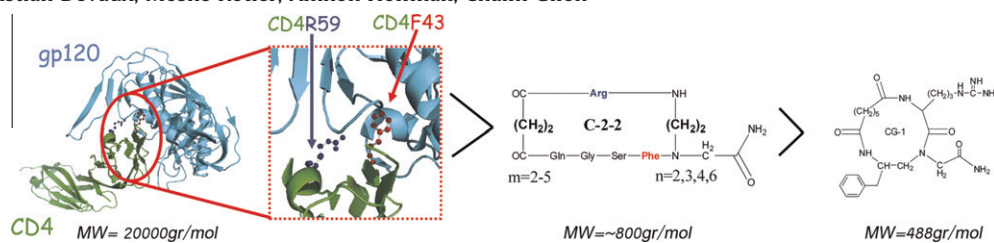
Spectrophotometry reveals noncooperative sequestration of Fe(III) by this multivalent, macromolecular compound.





**Rational conversion of noncontinuous active region in proteins into a small orally bioavailable macrocyclic drug-like molecule: The HIV-1 CD4:gp120 paradigm pp 5754–5761**

Mattan Hurevich\*, Avi Swed, Salim Joubran, Shira Cohen, Noam S. Freeman, Elena Britan-Rosich, Laurence Briant-Longuet, Martine Bardy, Christian Devaux, Moshe Kotler, Amnon Hoffman, Chaim Gilon\*



Screening of backbone cyclic peptide library: an intermediate step in rational design of orally available macrocyclic HIV-1 infection inhibitor that mimics gp120 binding site in CD4.



\*Corresponding author

Supplementary data available via ScienceDirect

**COVER**

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (<http://www.pymol.org>). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, 102, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, 61(6), 355–360].

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