CHEMMEDCHEM

CHEMISTRY ENABLING DRUG DISCOVERY

12/2006

http://www.chemmedchem.org

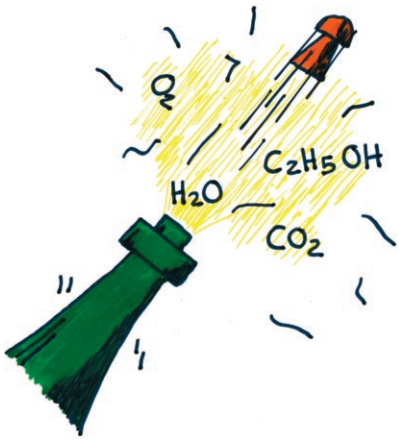
Full text:

WILEY InterScience® DISCOVER SOMETHING GREAT

http://www.interscience.wiley.com

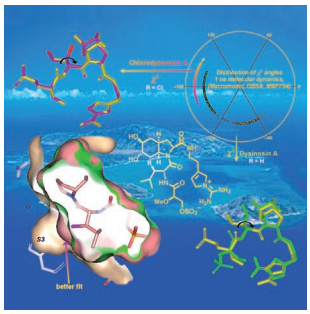
ChemMedChem, European in origin but international in scope, deals with all aspects of drug discovery. It is co-owned by a group of European chemical societies and is published by Wiley-VCH. Contributions in *ChemMedChem* cover medicinal and pharmaceutical sciences, drug design, drug development and delivery, molecular modeling, combinatorial chemistry, target validation, lead generation, and ADMET studies, that is, research from the overlapping areas between biology, chemistry, and medicine. *ChemMedChem* publishes Communications and Full Papers, as well as Reviews, Minireviews, Highlights, Concepts, Essays, Book Reviews, and occasionally Conference Reports. Authors can submit manuscripts to *ChemMedChem* online through our homepage (see left) by clicking on "Online Submission" and following the simple instructions.

Some articles in this issue have already appeared online in Wiley InterScience. See www.chemmedchem.org under EarlyView®



The editorial staff and the publishers thank all readers, authors, referees, and advertisers for their interest and support over the past year and wish them all a Happy New Year.

COVER PICTURE

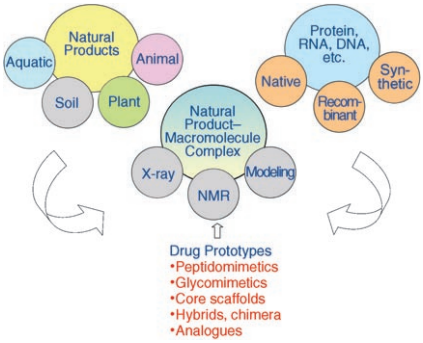


The cover picture shows the cyanobacterial linear peptides dysinosin A (R=H) and chlorodysinosin A (R=Cl), members of the aeruginosin family of cyanobacterial linear peptides. Their structures and absolute configurations were determined by total synthesis and X-ray co-crystallization with the enzyme thrombin. The presence of one chlorine atom in the D-leucine residue of chlorodysinosin A remarkably increases the inhibition potency against thrombin and Factor VIIa relative to dysinosin A. Molecular mechanics simulations starting from the bound conformations of dysinosin A and its chloro analogue suggest a more restricted sampling of conformations for the latter around the χ^1 dihedral angle. The chlorine atom in chlorodysinosin A may also contribute to lipophilicity, leading to a better fit in the hydrophobic S_3 pocket, as illustrated in the partial X-ray co-crystal structure. The background of the picture shows Lizard Island in North Queensland, Australia, where dysinosin A was isolated from the Dysideidae family of marine sponges. For details, see the Review by S. Hanessian on p. 1300 ff.

© 2006 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

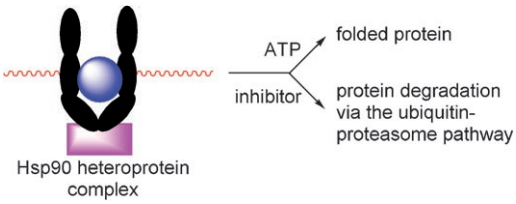
NEWS

REVIEWS



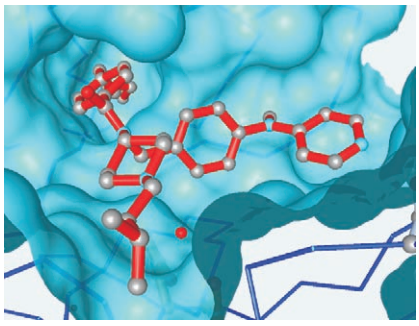
A "reorientation" of the concept of total synthesis of natural products emphasizes a biology-inspired, chemistry-driven approach without compromising the sanctity of basic research and the noble objectives of co-worker training in an academic setting. Structure-based organic synthesis provides a unique framework to capitalize on data gleaned from the bioactivity of natural products in conjunction with X-ray crystallography, molecular modeling, and NMR spectroscopy for the design and synthesis of new drug prototypes.

MINIREVIEWS



Blocking the chaperones: Heat shock protein 90 (Hsp90) has emerged as a promising target for the treatment of cancer, Alzheimer's and Parkinson's diseases, motor impairments, multiple sclerosis, and other disorders. Progress toward the development of both N- and C-terminal inhibitors is described.

COMMUNICATIONS

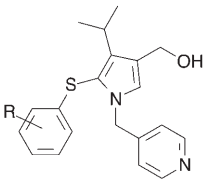


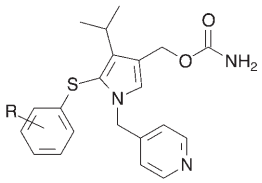
A novel class of molecules targeting aspartic proteinases from *P. falciparum* is described. Synthesis of these easily available, achiral, and highly potent molecules was supported by structural information and eventually allowed the identification of compounds highly active against three vacuolar aspartic proteinases. In a red blood cell assay, the growth of *P. falciparum* (strain K1) could be effectively prevented.

 © 2006 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

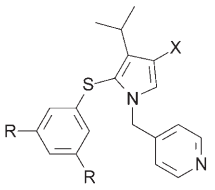
FULL PAPERS

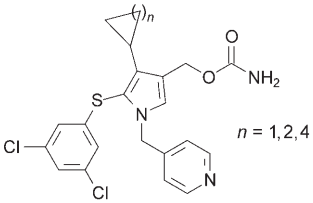
 © 2006 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim





AThPs are potent anti-HIV-1 agents that target reverse transcriptase. Compounds such as those shown are highly active against HIV-1 in cell-based assays. Moreover, selected derivatives showed interesting activities against clinically relevant, drug-resistant RT forms carrying K103N and Y181I mutations. Docking experiments were also performed to rationalize some SARs and resistance data.





AThPs are potent NNRTIs endowed with antiviral activities in cell-based assays. The effect of substitution at positions 3 and 4 of the pyrrole ring (examples shown) toward biological properties was studied, and the most active derivatives showed interesting activities against clinically relevant, drug-resistant RT forms (K103N, Y181I, and L100I). Docking simulations helped to explain some SAR and resistance data.

Supporting information on the WWW (see article for access details).

* Author to whom correspondence should be addressed.

SERVICE

All the Tables of Contents may be found on the WWW under: http://www.chemmedchem.org

Issue 11, 2006, was published online on October 31, 2006.

RSS Feed

Journal content prior to publication in an issue can be found online on our **Early View** page at www.chemmedchem.org. Stay updated on the latest journal content by registering for our **free e-mail alerts** at http://interscience.wiley.com/alerts.

Keep up with the latest research with our **RSS feed**, which provides the titles, authors, and the Digital Object Identifiers (DOIs) of Early View articles, including links to the full texts. RSS ("Really Simple Syndication") is an XML-based format for sharing and distributing web content. To receive the RSS feed, just click on the orange feed icon at www.chemmedchem.org, and visit http://interscience.wiley.com/rss for more information.

 © 2006 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim