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

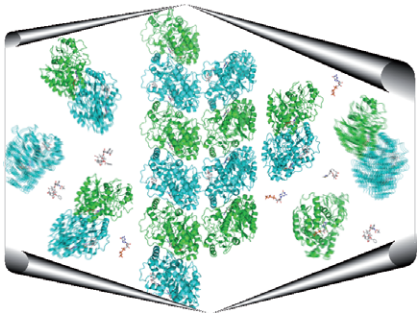
COVER PICTURE

The cover picture shows a human affected with malaria, the disease vector *Anopheles*, a map from the WHO showing areas of malaria risk, and MAP-412, an antimalarial compound developed in our group. As the map shows, regions affected by malaria include a large proportion of developing countries. Therefore, there is a need for new antimalarials that can be synthesized and supplied inexpensively. Prepared in just two steps from an inexpensive starting material, isonicotinic acid, our bis-cationic antimalarial compounds may be useful as leads for inexpensive antimalarials. For details, see the Full Paper by H. Kakuta et al. on p. 1527 ff. (Cover design by H.K.)

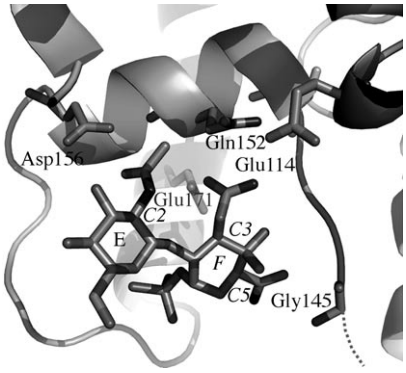
NEWS

REVIEWS

Computational tools are available that can increase the information content of experimentally determined structures far beyond gap filling, minor local conformational changes, and energy refinement.

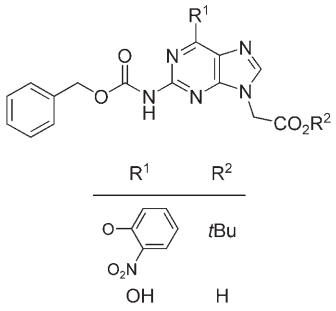


HIGHLIGHTS

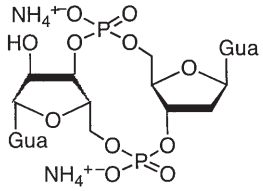


The recent publication by Strynadka and colleagues, describing the first X-ray structures of a soluble truncated version of PBP2 containing both glycosyltransferase and transpeptidase domains facilitates more common and feasible approaches for the rational design and in turn clinically useful GT-inhibitors for the treatment of infections caused by highly resistant bacterial organisms.

COMMUNICATIONS

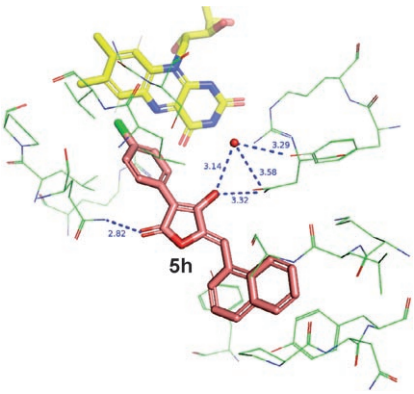


Beating the RT mutants: A novel class of N^2-Cbz-guan-9-yl acetic acid derivatives is endowed with anti-HIV-1 reverse transcriptase (RT) activity in the low micromolar range. These compounds have improved efficacy towards drug-resistant RT mutants relative to nevirapine and efavirenz. Their unique scaffold and interesting resistance profiles warrant further development.



***c*-dGpGp**

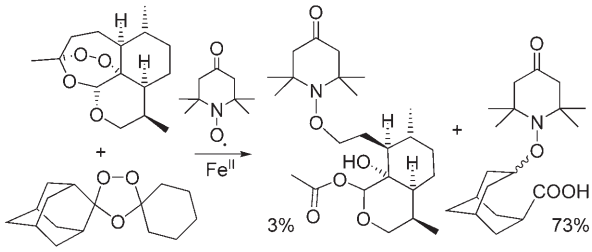
***c*-di-GMP** is considered to play an important role in regulating exopolysaccharide production, biofilm formation, and other phenotypes in bacteria. These attractive biological properties of *c*-di-GMP prompted us to carry out a systematic study of the bioactivity of *c*-di-GMP-related compounds, including derivatives with modified nucleoside bases, carbohydrates, or internucleotide bonds. Synthesis of c-dGpGp and its biological activities is reported.



A pathway screen targeting multiple muramyl peptide synthesis inhibitors identified the naphthyl tetronic acids series. Optimization of this series based on IC_{50}, K_d and MIC values led to potent inhibitors. Compound **5h** was co-crystallized in the active site of *E. coli* Mur B.

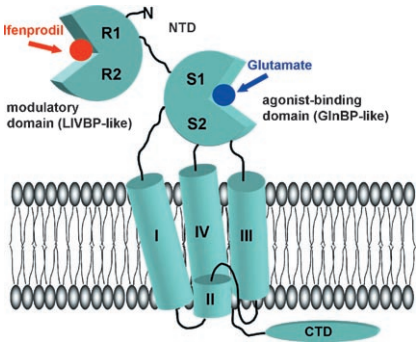
FULL PAPERS

R. K. Haynes, W. C. Chan, C.-M. Lung, A.-C. Uhlemann, U. Eckstein, D. Taramelli, S. Parapini, D. Monti, S. Krishna**



The Fe^{2+}-induced decomposition of artemisinins in relation to the ability to intercept C radical intermediates, their antimalarial activities, inhibition of the parasite PfATP6, and the effect of ascorbate and the iron chelator DFO on the biological properties have been examined. The artemisinins are intrinsically incapable of providing C radicals eminently suited for intermolecular reactions.

L. Marinelli, S. Cosconati, T. Steinbrecher, V. Limongelli, A. Bertamino, E. Novellino, D. A. Case*

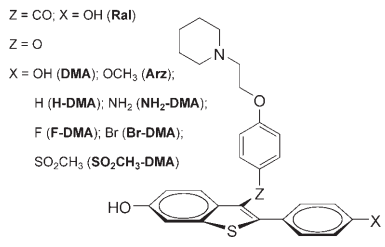


Open or closed? The construction of a 3D model for the NMDA NR2B domain is described along with docking, MD simulations, and MM-PBSA analysis. These calculations allowed the definition of ifenprodil binding pose at an atomic level in both the open and closed conformation of the NR2B domain. Finally, a hypothesis of the ifenprodil mechanism of action is proposed.

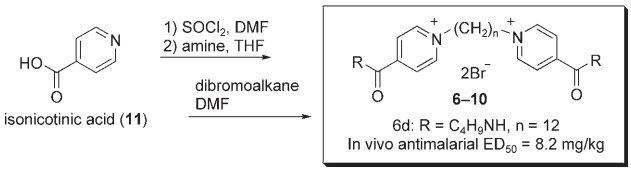
L. Gomez-Paloma, I. Bruno, E. Cini, S. Khochbin, M. Rodriquez, M. Taddei, S. Terracciano, K. Sadoul*

FR235222, one of the most potent HDAC inhibitors, is a natural tetrapeptide formed by some not easily available amino acids. We found that it is possible to build a structurally similar tetrapeptide made with simpler amino acids but maintaining Ahoda (indispensable) which has the high activity of the parent natural product and shows selective inhibition of class 1 histone deacetylase.

*C. R. Overk, K.-W. Peng, R. T. Asghodom, I. Kastrati, D. D. Lantvit, Z. Qin, J. Frasor, J. L. Bolton, G. R. J. Thatcher**



The ideal estrogen receptor modulator. Development of the "ideal" selective estrogen receptor modulator (SERM) is of importance in postmenopausal women's health. SERMs are generally oxidatively labile phenolic aromatics. Modification of the 4′-position of benzothiophene SERMs can modulate lability, but can the appropriate antiestrogenic profile be retained?



Managing malaria. As the area affected by malaria includes a large proportion of developing countries, there is a need for new antimalarials that can be synthesized and supplied inexpensively. In this study, bis-cation dimers, MAP series **6**–**10** synthesized from an inexpensive isonicotinic acid (**11**) in just two steps, were designed. MAP-412 (**6d**) exhibited a potent in vivo antimalarial activity.

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

* Author to whom correspondence should be addressed.

COMMENTARY

BOOKS

SERVICE

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