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CHEMICAL MEDICINAL CHEMISTRY

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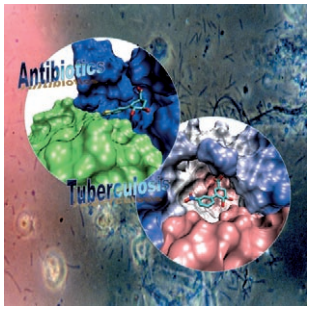
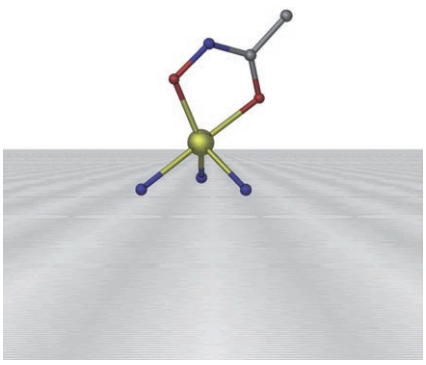
COVER PICTURE



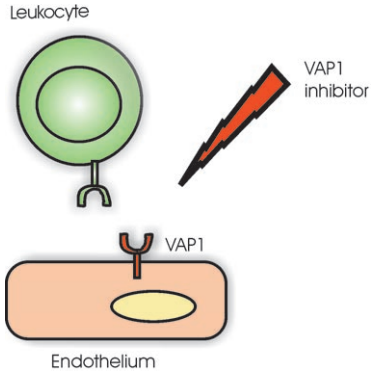
The cover picture shows two representations of two potent competitive inhibitors of *Mycobacterium tuberculosis* and *Streptomyces coelicolor* dehydroquinase with a bacterial culture in the background. These enzymes operate in the shikimic acid pathway, which is an important target for the development of new antibiotics. On the right, the bioactive conformation of the 3-nitrophenyl derivative as bound to the *Mycobacterium tuberculosis* active site, obtained from NMR spectroscopy, is highlighted. On the left, the picture depicts the proposed binding mode for the most potent inhibitor reported to date against any dehydroquinase, a 6-benzothiophenyl derivative (4 nM). For more details, see the Full Paper by C. González-Bello et al. on p. 194 ff.

NEWS

REVIEWS

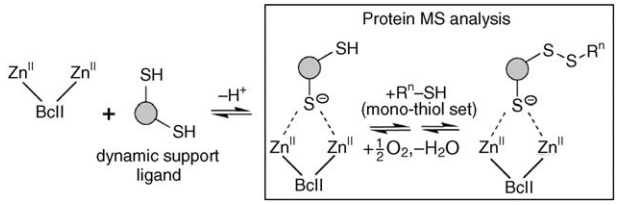


HIGHLIGHTS

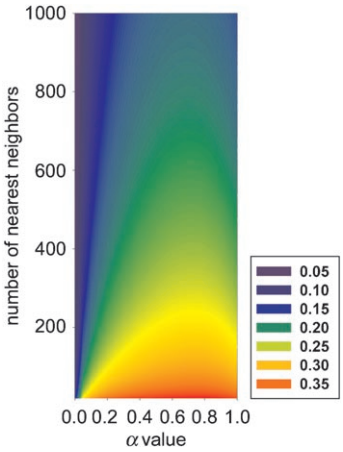


VAP1 as anti-inflammatory target: Over the last two years, small-molecule design in SSAO/VAP1 inhibitors has rapidly gained ground as an anti-inflammatory therapy. Small-molecule VAP1 inhibitors block SSAO enzymatic activity, thereby preventing leukocyte internalization through the endothelium. Thus, novel anti-adhesive molecules will allow the development of new anti-inflammatory compounds.

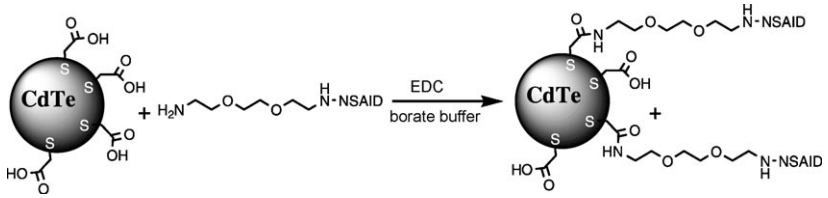
COMMUNICATIONS



An approach combining thiol based dynamic chemistry and MS was used to explore the SAR of a metallo-β-lactamase. Analogues of preferentially binding disulfides were synthesized and shown to be potent inhibitors.

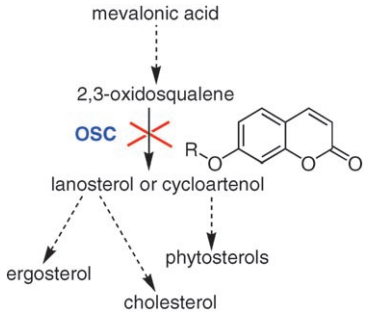


The power of asymmetry: Although symmetry is conceptually more beautiful, asymmetry can be more powerful in practice owing to the imperfectness of available information. We present evidence of asymmetry in pairwise chemical similarity measures by an empirical simulated similarity search based on two large pharmaceutical databases.

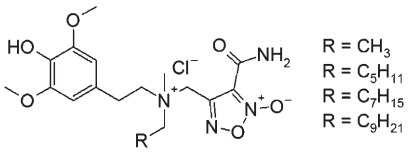


The first naproxen–QD conjugates have been synthesised and investigated. These conjugates demonstrated interesting photophysical properties, good stability in an aggressive enzymatic medium, and cellular localisation in macrophage (THP-1) cells. These nanocomposites might have the potential to act as drug delivery and cellular imaging agents.

FULL PAPERS



Five different oxidosqualene cyclases (OSCs) expressed in yeast, two of which from the pathogens *Trypanosoma cruzi* and *Pneumocycsis carinii*, were studied as targets of 18 coumarin derivatives prepared by unconventional synthetic procedures. Results show that this family of compounds has promise for the development of novel antiparasitic agents.



Models of amphiphilic NO-donor antioxidants were synthesized and studied for their antioxidant and vasodilator properties. Their ability to interact with phospholipid layers was investigated by NMR techniques. These compounds could be useful tools for pharmacological investigations.

BOOKS

SERVICE

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