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CHEMISTRY ENABLING DRUG DISCOVERY

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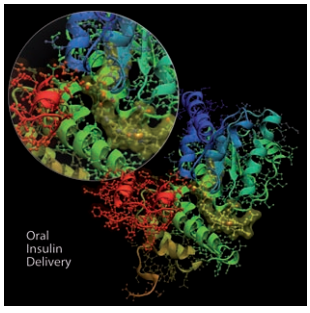
COVER PICTURE

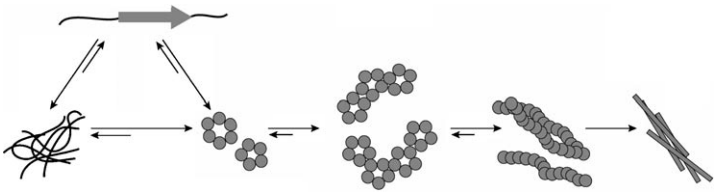


The cover picture shows an orally active, glucose-lowering vitamin B_{12}–insulin conjugate bound to the B_{12} uptake protein transcobalamin II (TCII). The inset shows a close-up view of the TCII binding pocket. (Insulin is in red; vitamin B_{12} is in bright yellow.) For details, see the Communication by T. J. Fairchild, R. P. Doyle, et al. on p. 1717 ff.

NEWS

REVIEWS

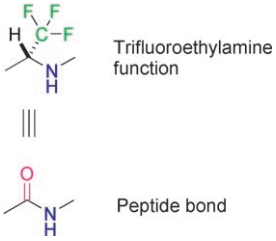
*C. I. Stains, K. Mondal, I. Ghosh**



Targeting amyloid. A review of molecules that target β-amyloid (Aβ) is presented. Particular attention is given to natural protein ligands, Aβ-derived peptides and peptidomimetics, anti-Aβ antibodies, in vitro anti-Aβ selected peptides and proteins, and small molecules that bind Aβ. Moreover, the described anti-amyloid molecular toolbox will also provide an avenue for the design of new diagnostic and therapeutic reagents.

MINIREVIEWS

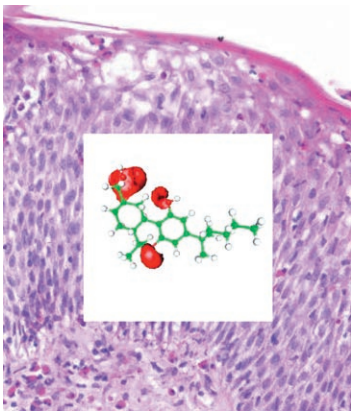
*M. Sani, A. Volonterio, M. Zanda**



3D instead of 2D. That's the main difference between the tetrahedral stereogenic trifluoroethylamine function and the planar peptide bond. This property, together with other remarkable features such as high metabolic stability and low basicity, turns out to be of great importance to allow trifluoroethylamines to be excellent peptide bond replacements.

HIGHLIGHTS

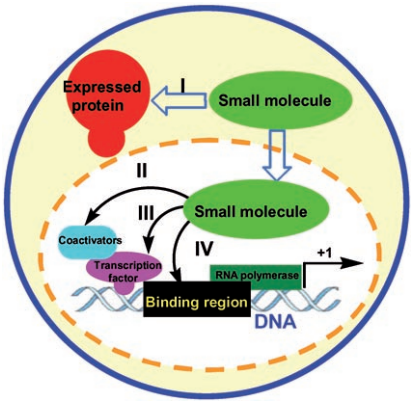
*D. M. Lambert**



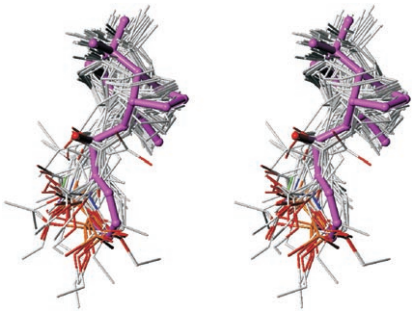
A therapeutic endocannabinoid-based strategy could be useful in numerous and diverse pathological conditions, including CNS disorders, cancer, and cardiovascular diseases. However, Karsak et al. have explored a poorly investigated area: the endocannabinoid system and its abilitly to elicit a protective role in allergic contact dermatitis. Herein, the significance of this work is discussed.

COMMUNICATIONS

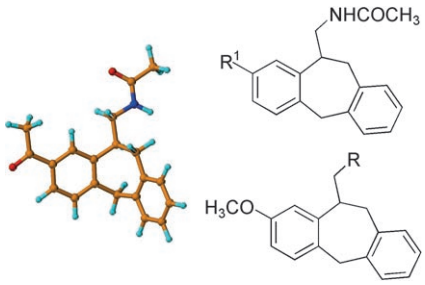
FULL PAPERS



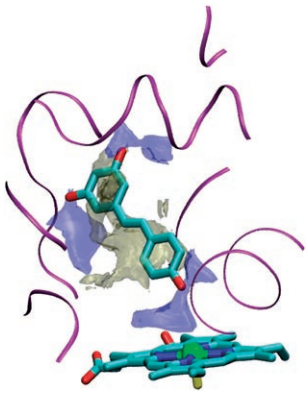
A grand challenge for chemical biologists involves the identification of small molecules that can effectively manipulate the transcription of encoded genes in cancer cells. Chiral *N*,*N*′-bis-salicyl diamino compounds have now been identified as an effective anticancer agent in the downregulation of Bcl-2 family gene expression in human breast cancer cells.



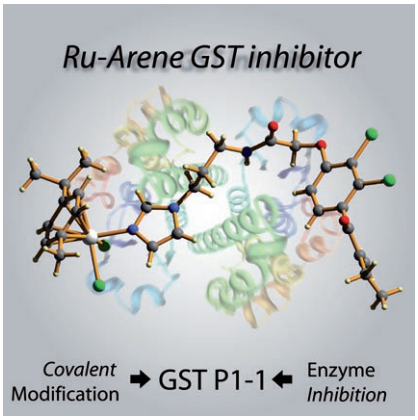
Detailed structure–activity relationships for the design of potent inhibitors for UGT isoforms have not been reported to date. This study provides a rational approach for the design of potent inhibitors for the UGT-isoform 2B7 based on the analysis of functional, stereochemical, and steric properties of a large set of tricyclic sesquiterpenoid derivatives.



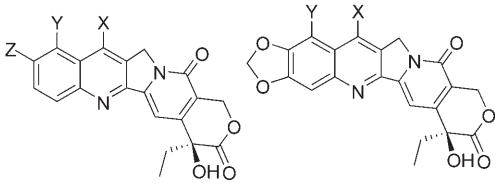
Tricyclic melatonin receptor antagonists: a series of MT_2 melatonin receptor antagonists, characterized by a 10,11-dihydro-5*H*-dibenzo[a,d]cycloheptene scaffold, were synthesized, and SARs were investigated. Enantiomeric resolution by MPLC allowed the testing of enantiomer selectivity, and docking studies with the MT_2 receptor suggested possible binding modes.



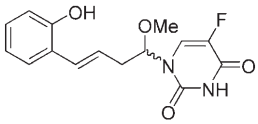
New strong aromatase inhibitors were identified experimentally. The physicochemical determinants for their productive binding to the active site of the enzyme were characterized through a combination of molecular modeling techniques based on grid-independent descriptors, molecular interaction fields and docking into the 3D homology model structure of the enzyme.



Two-pronged attack: By combining organometallic ruthenium fragments with ethacrynic acid, novel inhibitors of glutathione-*S*-transferase (GST) P1-1 were obtained. The complexes exhibit greater reactivity towards the enzyme and also represent potent anticancer compounds.



Revealing relationships: Quantitative structure–activity relationships were developed for two series of camptothecin derivatives with respect to their DNA topo I inhibition. The results show that these activities of camptothecin derivatives are largely dependent on the hydrophobic (and steric) properties of the molecules/substituents.



Looking for a differentiating agent. The concept of differentiation therapy is based on the conversion of malignant cells to a more benign phenotype using chemical substances. Compounds represented by the formula shown may be useful for differentiation therapy against the MCF-7 human breast cancer cell line.

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

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