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G-Protein-Coupled Receptors in Drug Discovery

Guest Editor: John Saunders

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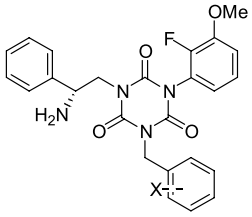
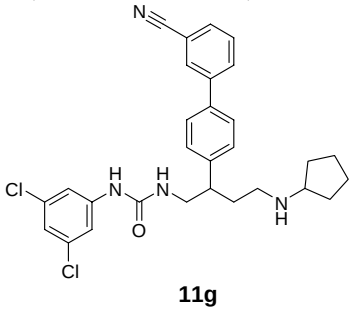
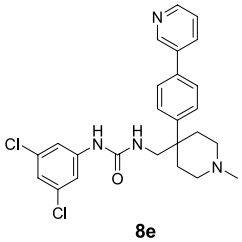


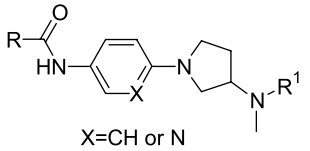
SAR studies of 1,3,5-triazine-2,4,6-triones as human gonadotropin-releasing receptor antagonists resulted in potent compounds. The best compound from the series had a binding affinity of 2 nM.



11g
MCH1R K_i = 3.0 nM



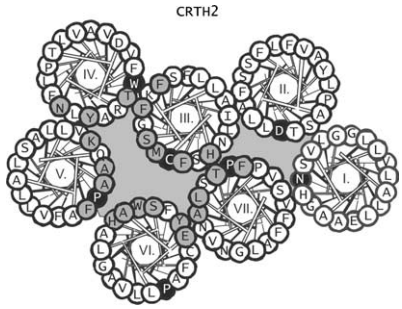
8e
MCH1R K_i = 3.1 nM

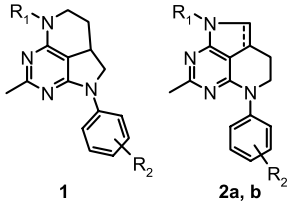


X=CH or N

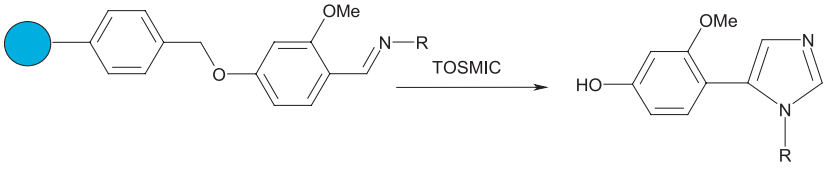
I

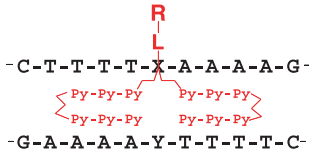
Derivatives of 1-(4-amino-phenyl)-pyrrolidin-3-yl-amine and 6-(3-amino-pyrrolidin-1-yl)-pyridin-3-yl-amine (**I**) were identified as potent and functionally active MCH receptor-1 (MCH-R1) antagonists. The compound **10** with K_i = 2.3 nM demonstrated good oral bioavailability (32%) and in vivo efficacy in rats.

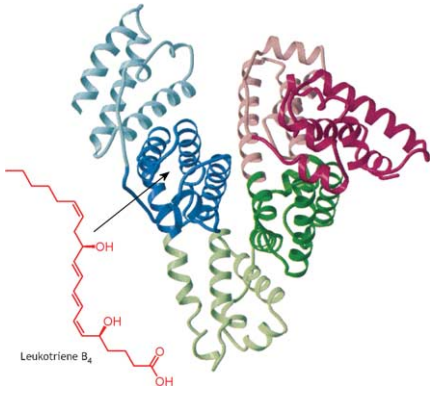


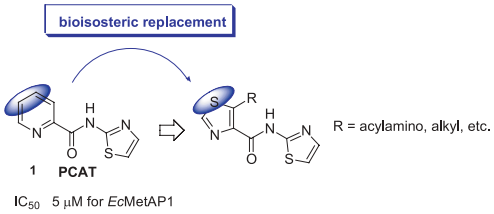


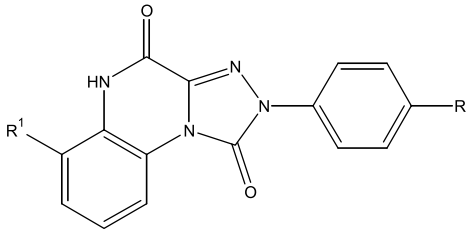
REGULAR COMMUNICATIONS

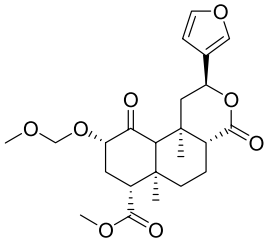




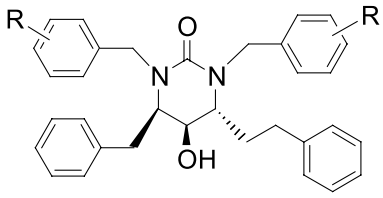






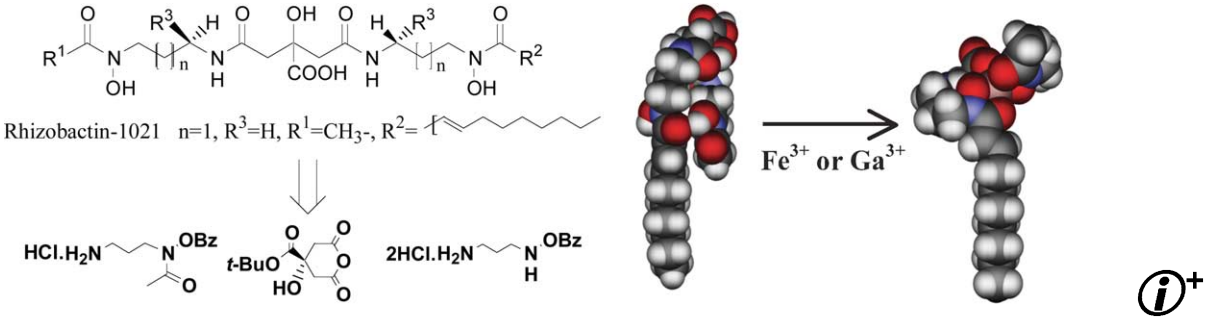


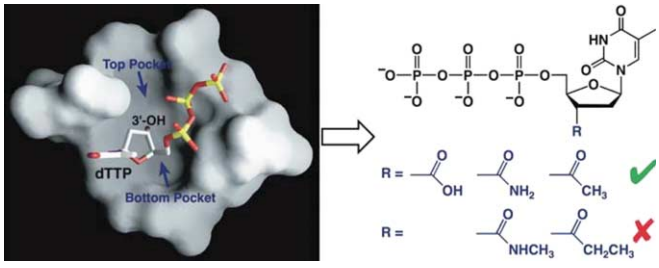
4 ED_{50} = 0.6 nM

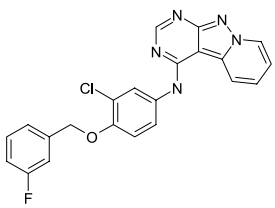


R=3- and/or 4 - CN, COOMe, OH, CH_2OH, NH_2, F, CH_2OH etc.

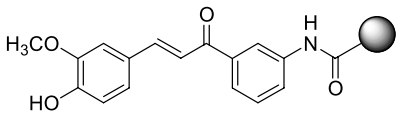
Balance of hydrophobicity and volume dependent polarizability has been found to play a key role in the inhibition of HIV protease by these inhibitors.



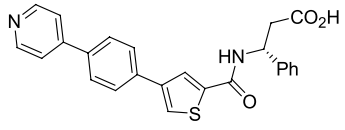




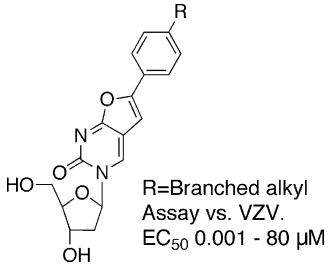
The discovery, synthesis, and in vitro kinase profile of several pyrido[1′,2′:1,5]pyrazolo[3,4-*d*]pyrimidines as potent kinase inhibitors are discussed.



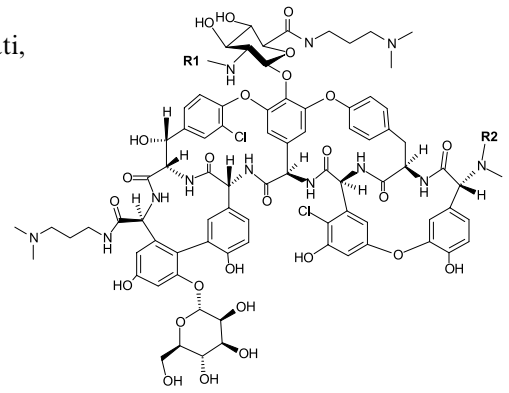
: alkyl, chloro-substituted phenyl and heteroaromatic



A new class of MMP-12 inhibitors was discovered and optimized using structure-based drug design methods. Optimization resulted in the discovery of a compound displaying nanomolar activity against MMP-12 which was co-crystallized with MMP-12.



The interaction of α-hydroxyl-containing organic radicals with B group vitamins is reported.



OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Schematic representation of the secondary structure elements of a rhodopsin-like 7TM receptor. The conserved key residues numbered according to the generic numbering system are highlighted in black. [Frimurer, T. M.; Ulven, T.; Elling, C. E.; Gerlach, L-O.; Kostenis, E.; Högberg, T. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3707.]

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