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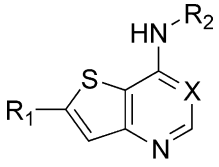
Bioorganic & Medicinal Chemistry Letters Vol. 14, No. 1, 2004

Bioorganic & Medicinal Chemistry Letters

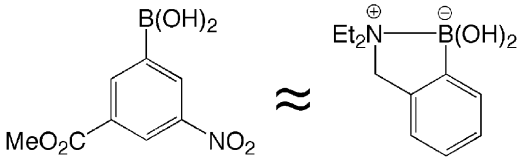
Contents

COMMUNICATIONS

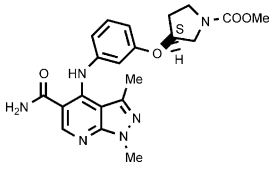


X = CH or N

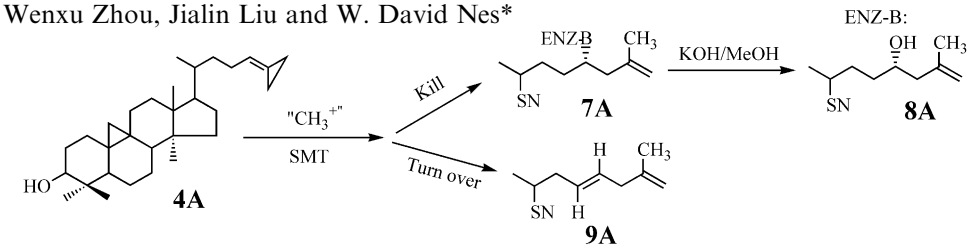
Novel thienopyrimidines and thienopyridines have been identified as potent inhibitors of VEGFR-2 kinase activity. The synthesis and SAR of these compounds is presented, highlighting our successful effort to diminish the EGFR kinase activity in the lead series.

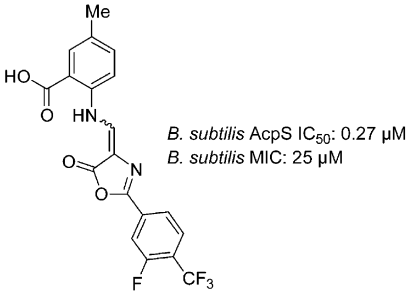


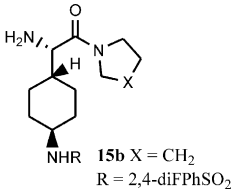
The nitro-boronic acid can be a substitute for the *ortho*-aminomethyl aryl-boronic acid motif for carbohydrate recognition.

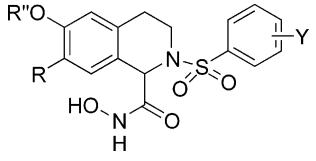


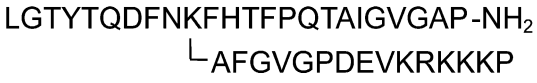
The discovery of an orally active pyrazolopyridine derivative as a structurally new PDE4 inhibitor is reported.



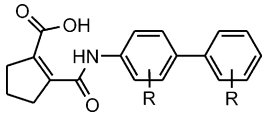




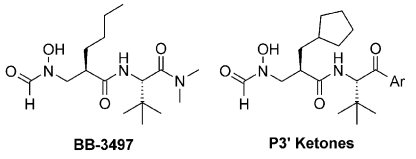




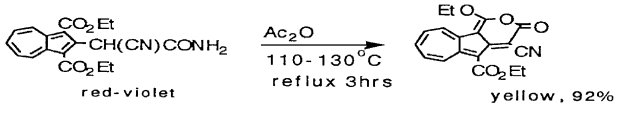
A novel hCT-derived carrier peptide was investigated for the cellular delivery of genes. This was demonstrated in in vitro-transfection assays with neuroblastoma cells SK-N-MC and a plasmid encoding for GFP.



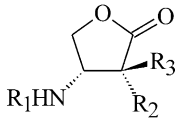
A novel series of DHODH inhibitors was developed, based on docking hits and medicinal chemistry exploration. The activity of the initial lead was improved by a QSAR method to yield low nanomolar inhibitors.



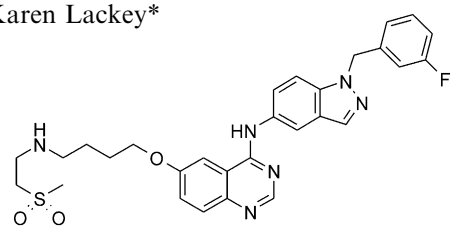
A series of analogues of the peptide deformylase (PDF) inhibitor BB-3497 where the P3′ amide bond was replaced with a ketone functionality is described. The in vitro antibacterial profiling of these compounds revealed that they demonstrate activity against pathogens associated with respiratory tract infections.



A facile method to synthesize 1-ethoxy-4-cyano-5-ethoxycarbonyl-3*H*-azuleno[1,2-*c*]pyran-3-one (in yield of 92%) which showed selective inhibition effect on 15-lipoxygenase(soybean source) at $IC_{50} = 24.2 \pm 2.7$ μM while no inhibition effect was observed at greater than 300 μM on 5-lipoxygenase, lipid peroxidase, phospholipase A_2, protein kinase C, and cyclooxygenase.

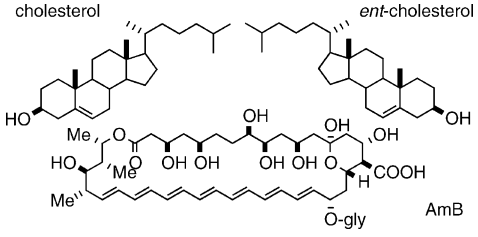


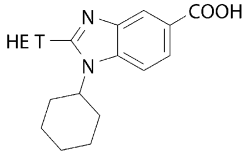
This report deals with the theoretical validation of the experimentally observed structure–activity relationships (SAR) of a set of *N*-substituted 4-amino-3,3-dialkyl-2(3*H*)-furanone GABA receptor modulators showing positive allosteric modulatory activity of the $GABA_A$ receptor similar to that shown by Loreclazole.



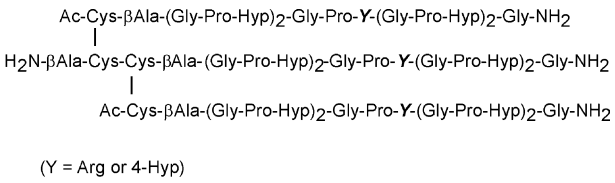
8f

A series of 6-alkoxy-4-anilinoquinazoline compounds was prepared and evaluated for in vitro inhibition of the erbB2 and EGFR kinase activity. The IC_{50} values of the best compounds were below 100 nM. Further, several of these compounds inhibit the growth of erbB2 and EGFR over-expressing tumor cell lines at concentrations below 1 uM.

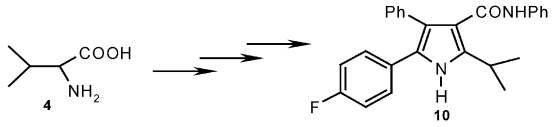




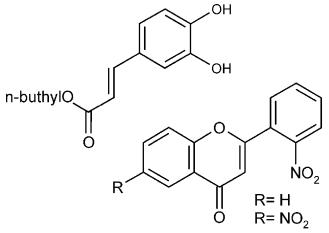
HCV NS5B polymerase:
IC_{50} = 1.6 μM (HET = 3-furyl)



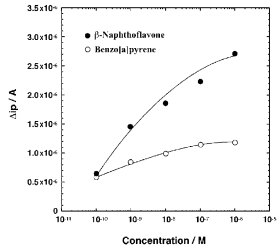
Heterotrimeric collagen-model peptides were synthesized. Effect of Arg residues on triple helical stability was examined.



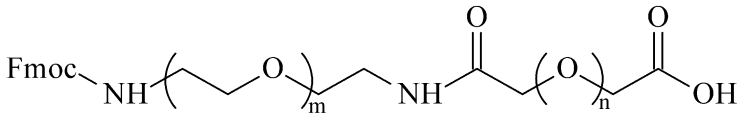
Atorvastatin intermediate **10** was synthesized from L-valine **4** via 1,3-dipolar cycloaddition reaction of mesoionic munchnone and *N*-debenzylation as key steps.



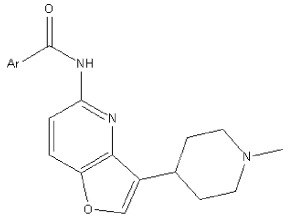
The effect of a series of natural and synthetic flavonoids and some related compounds on the proliferation of WISH cells is shown. 2′-Nitroflavone, 2′,6-dinitroflavone, and caffeic acid *n*-buthyl ester were the most active cytotoxic agents. When these derivatives were assayed in the presence of a suboptimal concentration of interferon-α2b, an additive effect on cell growth inhibition was observed.



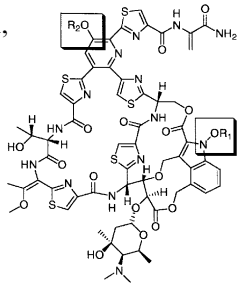
A bioaffinity sensor which carries the hAhR was developed aiming at the detection of PAHs.



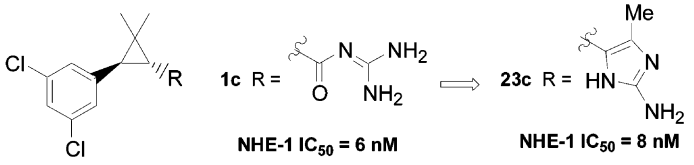
m = 1, 2; n = 0, 1



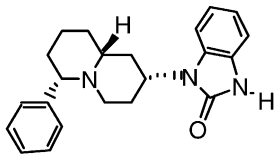
5,12,13,14



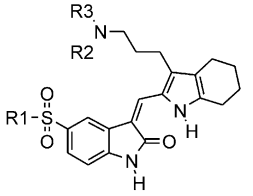
The semi-synthesis and antibacterial activity of *O*-alkyl nocathiacins derivatives are reported.

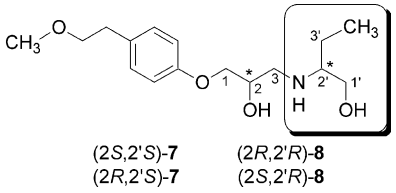


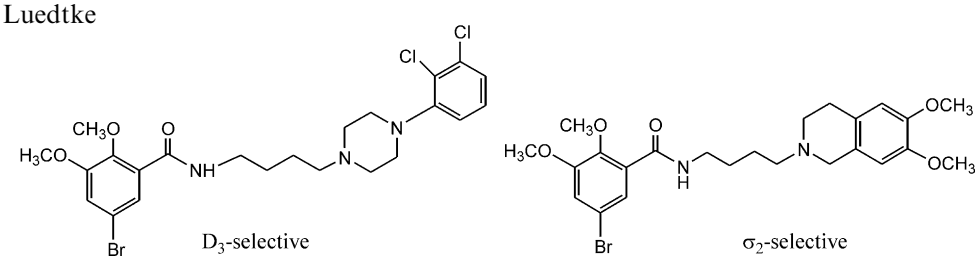
NHE-1 inhibitory activity of a series of heterocyclic cyclopropanes is described.



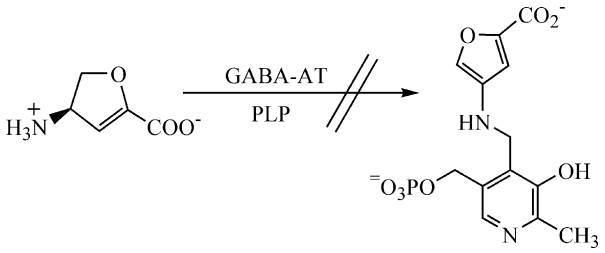
The design and synthesis of a novel scaffold for potent ORL1 and opioid ligands is described.

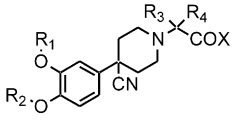




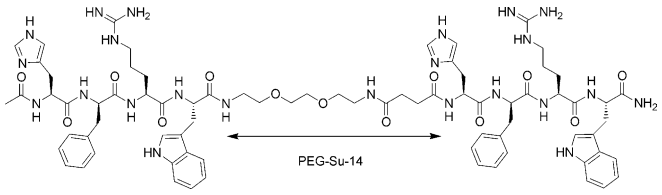


The synthesis of a series of conformationally-flexible benzamide analogues and their in vitro binding affinities for dopamine D_2, D_3, D_4 and sigma receptors are presented.

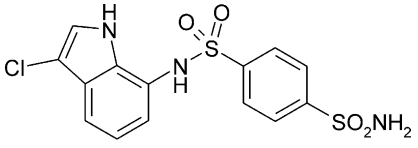


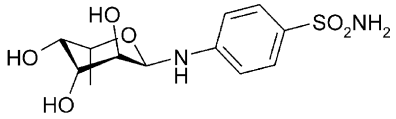


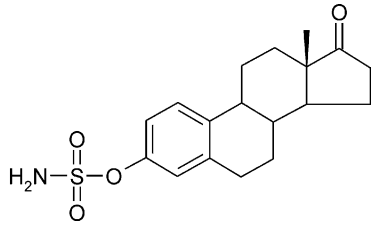
Synthesis and biological evaluation of piperidine derivatives is reported.

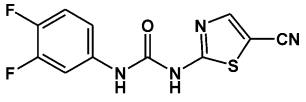


Homooligomers constructed with peptide fragments of melanocortin (α-MSH) bind with higher affinity and with apparent cooperativity to melanocortin receptor hMC4R, compared to their constituent monomers.



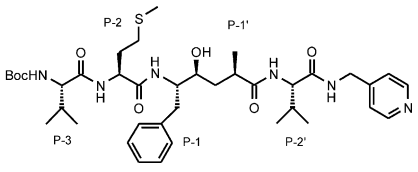




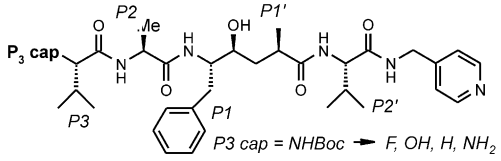


3p

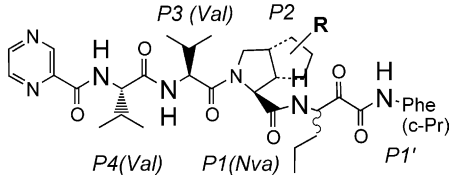
Over 50 phenyl thiazolyl urea and carbamate derivatives were synthesized for evaluation as new inhibitors of bacterial cell-wall biosynthesis. Many of them demonstrated good activity against MurA and MurB and gram-positive bacteria including MRSA, VRE and PRSP. 3,4-Difluorophenyl 5-cyanothiazolylurea (**3p**) with clog P of 2.64 demonstrated antibacterial activity against both gram-positive and gram-negative bacteria.



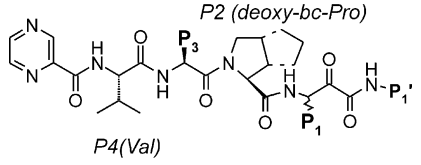
We describe herein the syntheses and evaluation of a series of Phe*-Ala-based BACE inhibitors. The most promising inhibitors demonstrated very good enzyme and cellular activity.



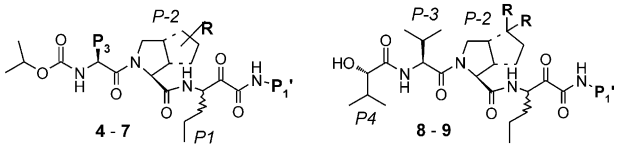
Several series of P3 cap modified BACE inhibitors were prepard in order to reduce M_r and adjust log D values of inhibitors for better BBB penetration. A number of P3 cap hydroxylated inhibitors showed good enzyme inhibitory and whole cell activities.



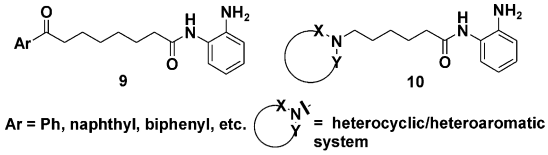
We describe herein the design, synthesis, and evaluation of a series of bicycloproline P2 bearing tetrapeptidyl α-ketoamides as HCV protease inhibitors.



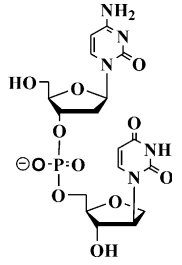
We describe herein the discovery of **LY526181**, a P2 bicycloproline tetrapeptidyl α-ketoamide HCV protease inhibitor with desirable antiviral activity, ADME and toxicological profile.



We describe herein the design, synthesis, antiviral activity and cytotoxicity of two series of tripeptidyl α-ketoamides based HCV protease inhibitors.



A series of benzamides (**9** and **10**) was synthesized and their biological evaluation as HDAC inhibitor is reported.



Remarkable resistance of synthetic dinucleotides towards exonucleases.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

*Cover figure provided by **Indraneel Ghosh**, Department of Chemistry, University of Arizona.* The cover depicts the **Dual Surface Selection** methodology developed by the author: the blue helix of htB1 (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htB1 (center) allows for functional selection against thrombin (right).

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ISSN 0960-894X