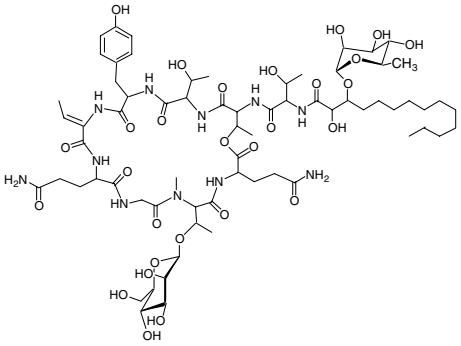
ELSEVIER

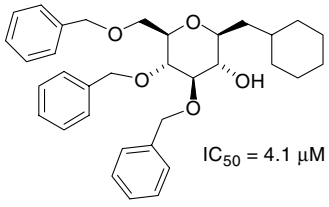
Bioorganic &
Medicinal
Chemistry
Letters

Bioorganic & Medicinal Chemistry Letters Vol. 16, No. 16, 2006

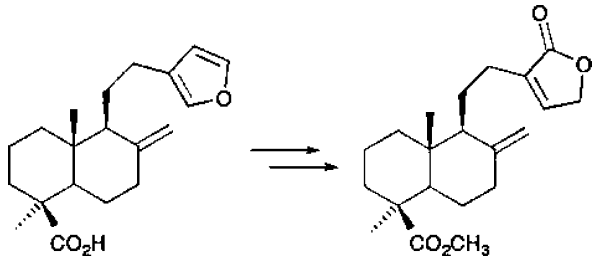
Contents

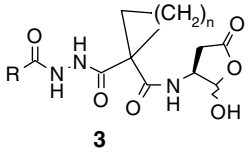
ARTICLES





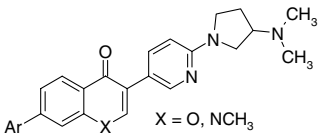
A large series of alkyl *C*-glycosides was synthesized and screened against the human promyelocytic leukemia cell line (HL60), showing significant activity and apoptosis.



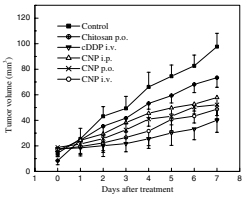


3

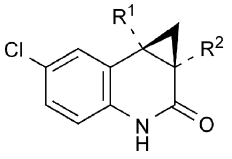
Novel 1-(2-acylhydrazinocarbonyl)cycloalkyl carboxamides were designed and synthesized as selective peptidomimetic inhibitors of interleukin-1β converting enzyme (ICE IC_{50} values <100 nM).



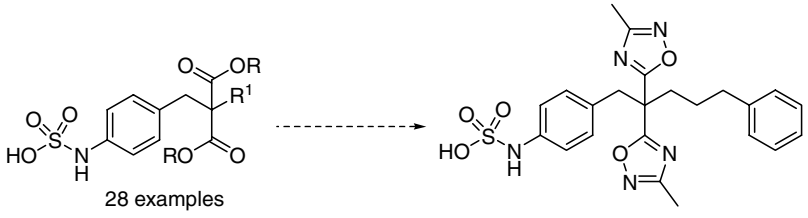
A series of substituted chromones were designed, synthesized, and evaluated for their ability to bind melanin-concentrating hormone receptor 1. Compounds with subnanomolar binding affinity and 66% oral bioavailability in rats were discovered.

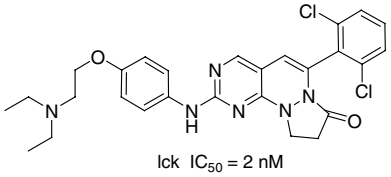


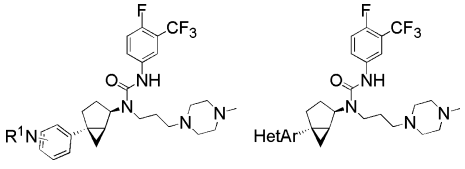
Effects of administration routes on antitumor efficacy of chitosan nanoparticles (CNP) against Sarcoma-180 subcutaneous tumor formation and growth in ICR mice.



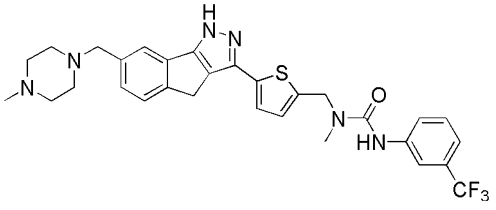
Novel HIV-1 non-nucleoside reverse transcriptase inhibitors

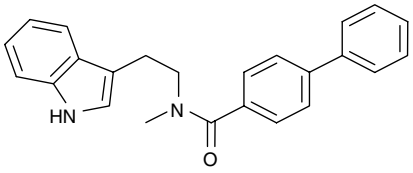






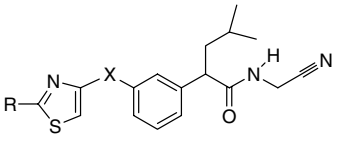
A series of 1,4-dihydroindeno[1,2-*c*]pyrazoles with urea-type side chains was identified as potent multitargeted (VEGFR and PDGFR families) receptor tyrosine kinase inhibitors. A KDR homology model suggested that the urea moiety is able to interact with a recognition motif in the hydrophobic specificity pocket of the enzyme.





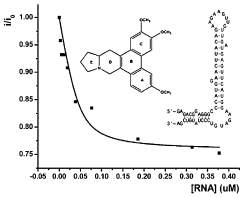
CA224

CA224, a tryptamine analogue of fascaplysin, is a specific inhibitor of Cdk4-D1 against Cdk2-A in enzyme assays, blocks cancer cells at G_0/G_1 and prevents pRB hyperphosphorylation, but does not bind or intercalate DNA like fascaplysin.



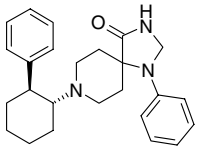
X: phenyl ring

A novel series of potent and selective inhibitors of cysteine protease cathepsin K is described.

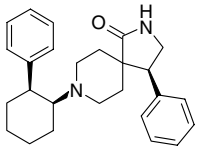


Tobacco mosaic virus (TMV) inhibitor tylophorine B binds to TMV RNA in multiple binding sites with IC_{50} of 2.4 nM. It also binds to assembly origin of TMV RNA with one binding site of K_d of 9 nM. We speculate that tylophorine B likely exerts its virus inhibition by binding to assembly origin, and interfering with virus assembly initiation.

A novel class of 4-substituted-8-(2-phenyl-cyclohexyl)-2,8-diaza-spiro[4.5]decan-1-ones have been discovered and developed as potent and selective GlyT1 inhibitors. The molecules display excellent selectivities (when compared to their triazaspiropiperidine analogues) against the μ opioid receptor as well as the nociceptin/orphanin FQ peptide (NOP) receptor.

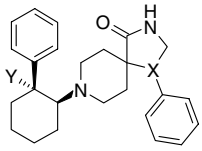


GlyT1 EC_{50} (μM): 0.073
NOP IC_{50} (μM): 0.310
μ IC_{50} (μM): 0.520

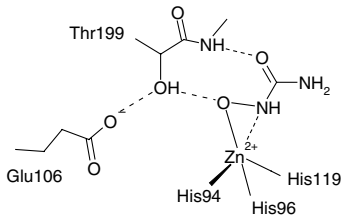


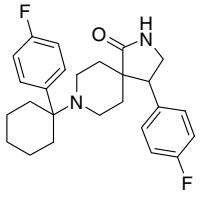
GlyT1 EC_{50} (μM): 0.246
NOP IC_{50} (μM): >10
μ IC_{50} (μM): >10

A novel class of 2,8-diaza-spiro[4.5]decan-1-ones have been discovered and developed as potent and selective GlyT1 inhibitors. In general, the diaspiropiperidine series show improved metabolic stability (when compared to the triazaspiropiperidine series) and we have also identified a key relationship between reducing basicity of the piperidine nitrogen and reducing hERG affinity.

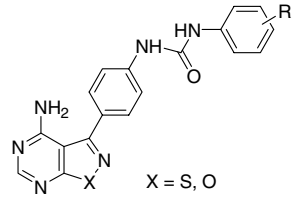


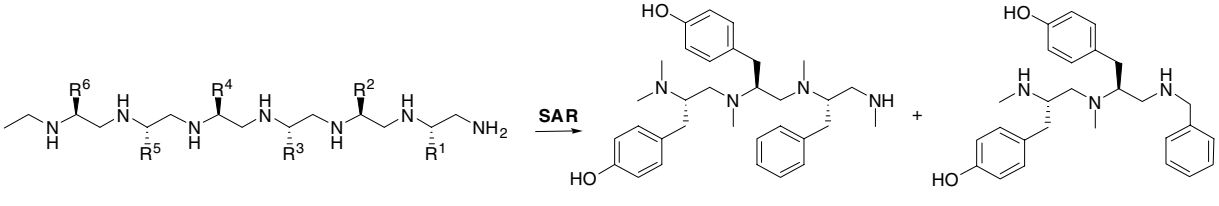
X = N; Y = H: CL_{int} (μL/min/mg protein): 240
X = N; Y = OH: CL_{int} (μL/min/mg protein): 499
X = CH; Y = H: CL_{int} (μL/min/mg protein): 36
X = CH; Y = OH: CL_{int} (μL/min/mg protein): 13





GlyT1 EC_{50} (μM): 0.095

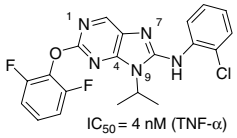


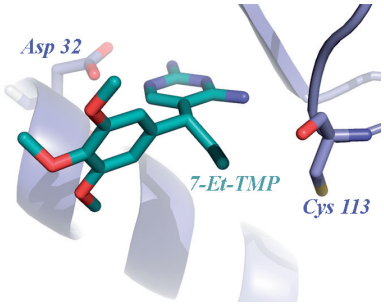


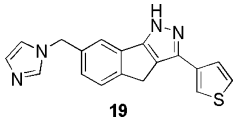
μ opioid receptor: IC_{50} = 0.5 nM

μ opioid receptor : IC_{50} = 2 nM

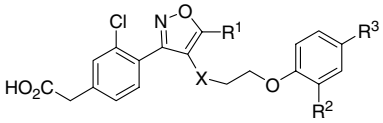
Screening of a mixture based heptaamine library (34,012,170 compounds) against μ opioid receptor and identification of highly active heptaamine compounds.

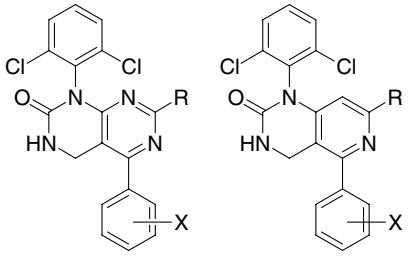


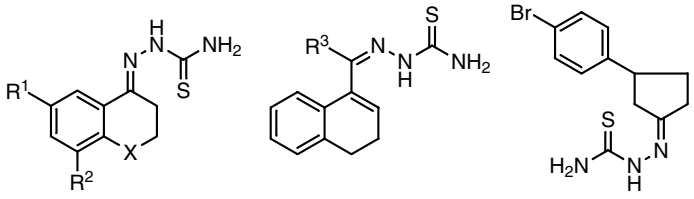


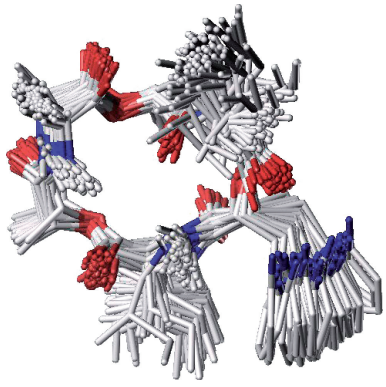


19

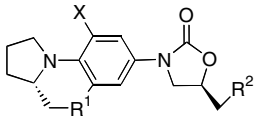




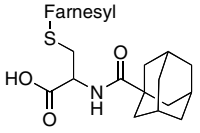




The substituted (*R*)-phenyllactic acid containing cyclohexadepsipeptides (CHDPs) **3**–**7** represent novel enniatin derivatives with strong in vivo activities against the parasitic nematode *Haemonchus contortus* Rudolphi in sheep. 2D NMR spectroscopic analysis revealed for the substituted (*R*)-phenyllactic acid containing CHDPs one major conformer with an unsymmetrically folded conformation lacking a *cis*-amide bond. A correlation between the substitution pattern and its anthelmintic activity was found. Here we report on a simple total synthetic pathway of the precursor for this particular type of CHDPs and an efficient modification of the benzylic side chain (*R*-PhLac^2).



The synthesis of a series of tricyclic oxazolidinones employing a tandem SN_2 and SNAr reaction as the key step is disclosed. SAR studies on these novel compounds resulted in certain potent antibacterial compounds.



7c
IC_{50} = 12.4 μM

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

View of the crystal structure of the DB819-d(CGCGAATTCGCG)$_2$ complex, looking down the minor groove of the DNA (see Campbell, N.H.; Evans, D.A.; Lee, M.P.H.; Parkinson, G.N.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 15). The DB819 molecule is shown in space-filling mode. Visualisation produced with the VMD program. [Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* **1996**, *14*, 33.]

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

ELSEVIER

ISSN 0960-894X