Contents lists available at ScienceDirect

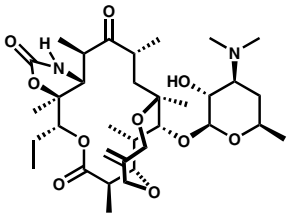
Bioorganic & Medicinal Chemistry Letters

journal homepage: www.elsevier.com/locate/bmcl

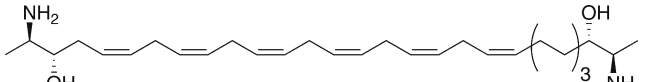
Bioorganic & Medicinal Chemistry Letters Vol. 18, No. 24, 2008

Contents

ARTICLES

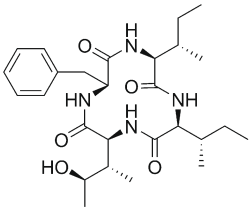


The synthesis of 3,6-bicyclolides from erythromycin A oxime is described. This novel class of bridged bicyclic macrolides demonstrates potent in vitro and in vivo activities against a broad spectrum of bacteria including resistant respiratory tract pathogens.

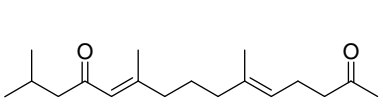


Leucettamol A

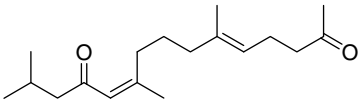
Leucettamol A is the first inhibitor of Ubc13-Uev1A interaction. Such inhibitors are presumed to be leads for anti-cancer agents that upregulate activity of the tumor suppressor p53 protein.



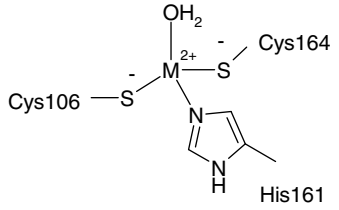
WSS2219
a selective inhibitor of GlyT1
IC_{50} = 3.0 nM



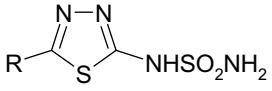
(5*E*,10*E*)-6,10,14-trimethylpentadeca-5,10-diene-2,12-dione(**311**)



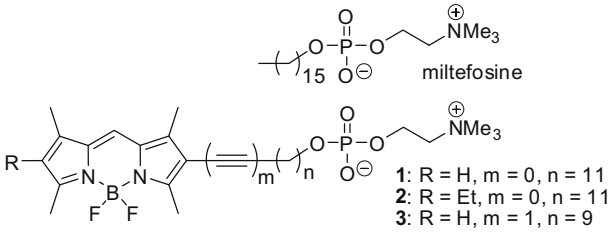
(5*E*,10*Z*)-6,10,14-trimethylpentadeca-5,10-diene-2,12-dione(**312**)



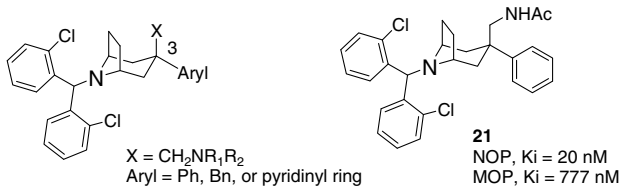
K_I (iodide) = 10.3 μM, K_I (sulfamide) = 8.7 μM



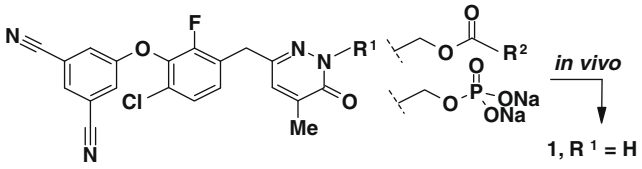
K_I = 4.2 – 32 nM (hCA VA)
K_I = 1.3 – 74 nM (hCA VB)



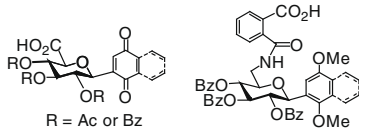
Highly fluorescent and photostable analogues of the leishmanicidal drug miltefosine have been prepared, in which the antiparasite activity has been preserved.



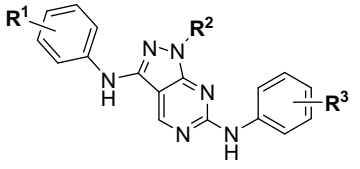
A series of 3-disubstituted-nortropane analogs have been identified to bind to the nociceptin receptor with high affinity. The syntheses and structure–activity relationships of these analogs are described.



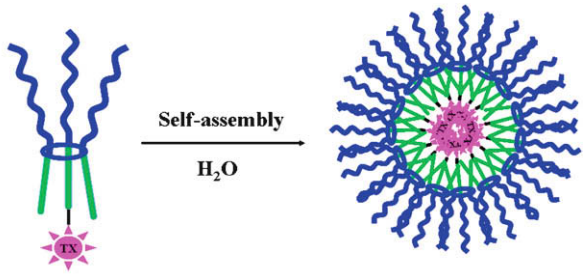
Pyridazinone **1** was derivatized into a series of hydroxymethyl esters, carbonates and one phosphate. These prodrugs were orally dosed to rats and afforded increases of 4.3- to 8.6-fold in 24-hour exposure of **1** (over that of parent) and not detected in blood plasma.



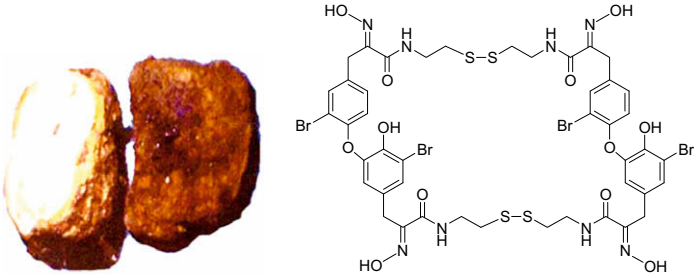
Benzoyl protected β-*C*-glycosyl compounds inhibitent PTP1B with IC_{50} in micromolar range.



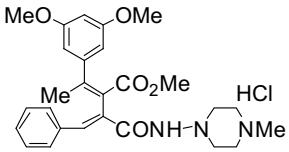
A new series of pyrazolo[3,4-*d*]pyrimidine-3,6-diamines was designed and synthesized as potent and selective inhibitors of the nonreceptor tyrosine kinase, ACK1. These compounds arose from efforts to rigidify an earlier series of *N*-aryl pyrimidine-5-carboxamides. The synthesis and structure–activity relationships of this new series of inhibitors are reported. The most promising compounds were also profiled for their pharmacokinetic properties.



A novel biodegradable micelle-forming cyclotriphosphazene–paclitaxel conjugate was synthesized.



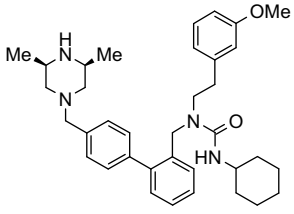
***Jaspis* sp. and *Poecillastra* sp.**



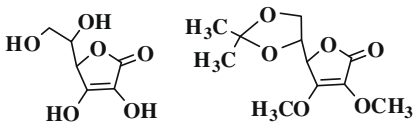
T-2639

The design, synthesis, and evaluation of T-2639, orally active inhibitor of PAI-1 production, is reported.

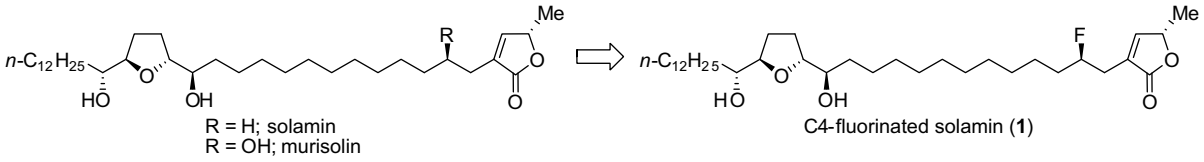
High-throughput screening resulted in the identification of a series of novel motilin receptor agonists with relatively low molecular weights. The series originated from an array of biphenyl derivatives designed to target 7-transmembrane (7-TM) receptors. Further investigation of the structure–activity relationship within the series resulted in the identification of compound (**22**) as a potent and selective agonist at the motilin receptor.



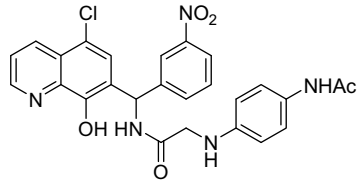
22

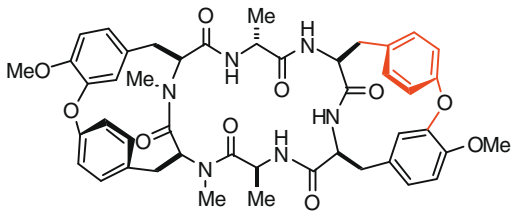


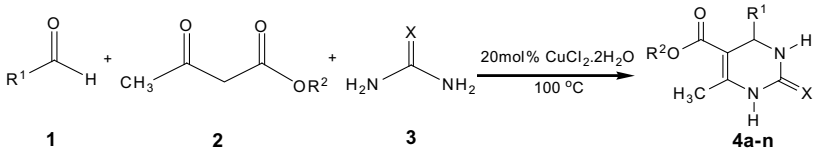
Effects of ascorbic acid and 5,6-*O*-isopropylidene-2,3-*O*-dimethylascorbic acid on final product formation in radiolysis of ethanol, aqueous solutions of ethanol, ethylene glycol, α-methylglycoside, maltose, α-glycerophosphate, and α-glucose phosphate were studied.



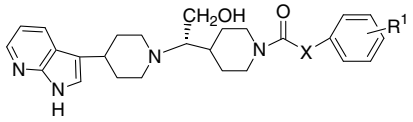
C4-Fluorinated analogues of solamin, an antitumor acetogenin, were synthesized and investigated for their growth inhibitory activity against 39 tumor cell lines.



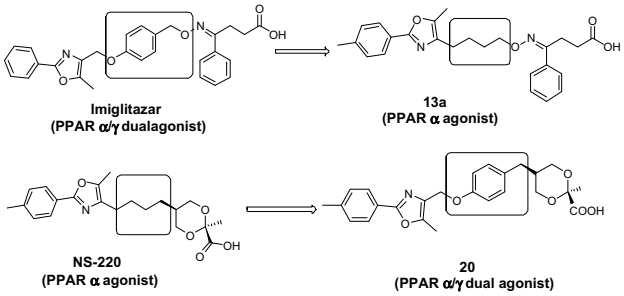


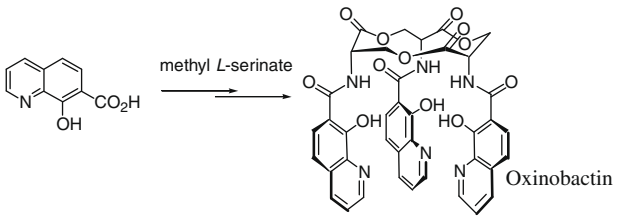


The synthesis of dihydropyridines under solvent-free conditions catalyzed by cupric chloride and their antifungal activities are reported.

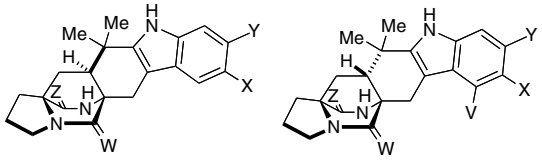


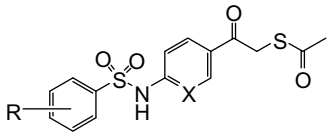
SAR studies led to the discovery of 7-azaindole piperidine derivatives as potent CCR2 antagonists displaying IC_{50} values in the nanomolar range.



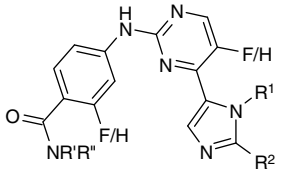


Synthesis of oxinobactin from 8-hydroxyquinoline and methyl-L-serinate. A new chiral siderophore analogue to enterobactin is reported and its iron complexing ability is evaluated by UV–vis spectrophotometric competitive studies.

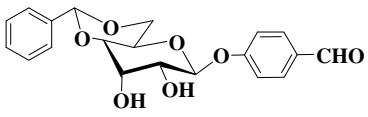




The identification and lead optimization of a novel series of α-mercaptoketone HDAC inhibitors is described.

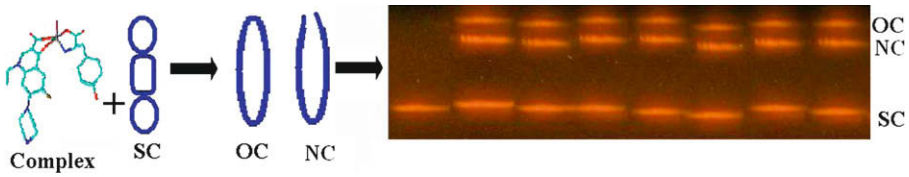


The SAR and optimisation of a novel series of imidazole pyrimidine amides is reported.

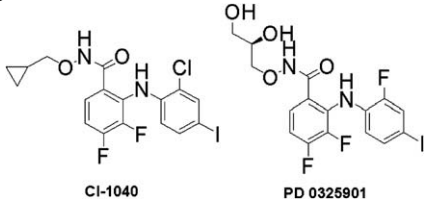


1c

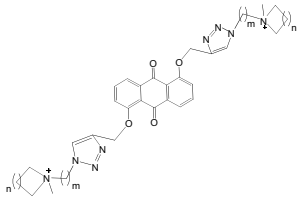
A series of helicid analogues were synthesized and their inhibitory activities on the diphenolase activity of mushroom tyrosinase were investigated. Compound **1c** was found to be the most potent compound with IC_{50} value of 0.052 mM.



Synthesis of oxovanadium (IV), ciprofloxacin, and aminoacids. All the compounds were screened for antimicrobial activity in vitro and nuclease activity. Complexes exhibit comparable MIC values than standard drugs.

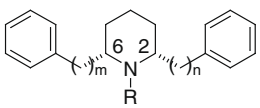


A novel series of benzhydroxamic esters were identified as potent MEK inhibitors. Optimization of these esters produced the two clinical candidates **CI-1040** and **PD 0325901**.



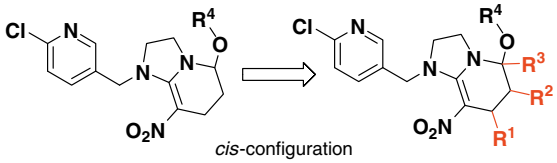
Compound **1**: m=3, n=0
Compound **2**: m=2, n=2
Compound **3**: m=2, n=3

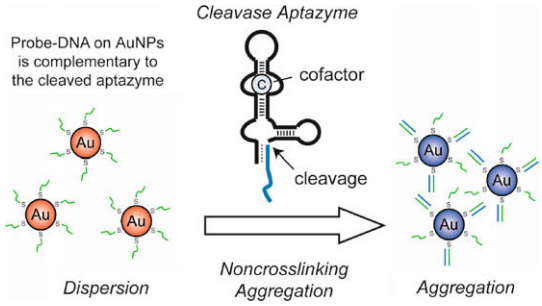
Three water soluble anthraquinone derivatives were synthesized via employing click chemistry and the mechanistic study of the apoptotic induction was conducted in this paper.



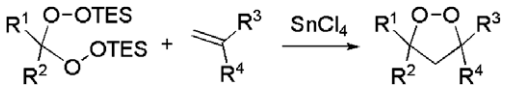
m = 0, 1, 2, or 3
n = 0, 1, 2, or 3
R = H or CH_3

A series of lobelane homologues has been synthesized and evaluated for their [^{3}H]DTBZ binding affinity at the vesicular monoamine transporter-2 (VMAT2). The structure–activity relationships (SAR) indicate that for retention of binding affinity at VMAT2, the lengths of the methylene linkers should be no shorter than one methylene unit at C-6 of the piperidine ring, and no shorter than two methylene units at C-2 of the piperidine ring. These results indicate that the intramolecular distances between the piperidine ring and two phenyl rings in lobelane analogues are an important criterion for retention of high affinity at VMAT2.

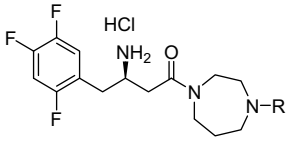


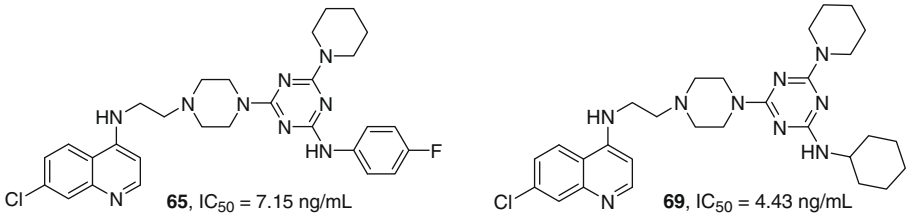


We easily detected cofactors of aptazymes using noncrosslinking gold nanoparticle aggregation.

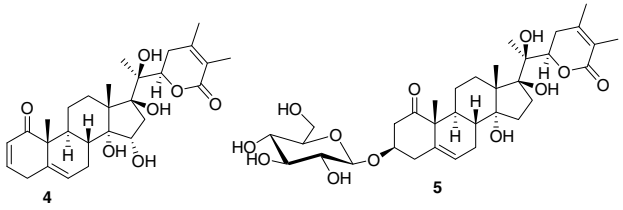


A $SnCl_4$-mediated annulation was utilized to form a series of 1,2-dioxolanes, which were tested for activity against multiple strains of *Plasmodium falciparum*.

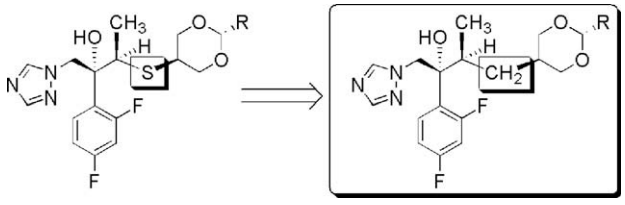




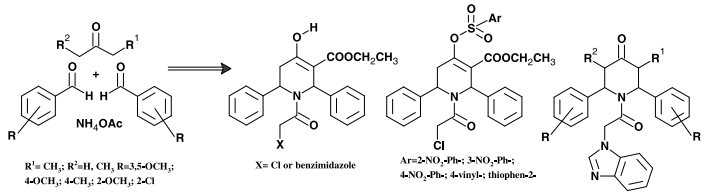
A series of new class of hybrid 4-aminoquinoline triazines were synthesized and screened against CQ sensitive strain 3D7 of *P. falciparum* in an in vitro model and CQ resistant strain N-67 of *P. yoelii* in an in vivo assay. The compounds **65** and **69** exhibited more than 99% suppression on day 4.



Isolation, structure elucidation of new compound **4** and antihyperglycemic activity of compounds **1**–**5** are reported.

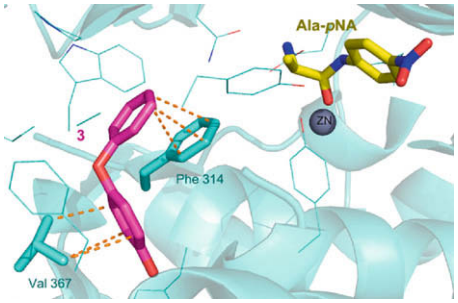


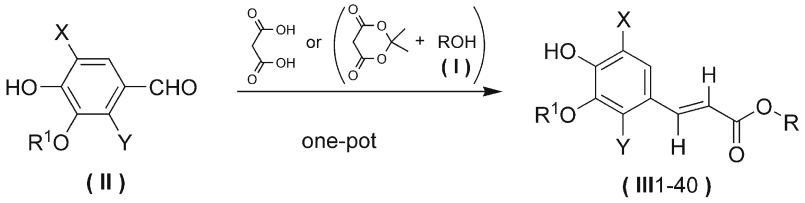
Stereoselective synthesis and in vitro antifungal activities of a novel series of triazole antifungal agents wherein the sulfur atom was replaced by a carbon atom are described.



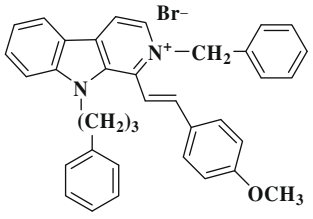
A series of substituted piperidones and tetrahydropyridine sulfonates were synthesized and explored for their antibacterial activities against sensitive and resistant organisms besides their antitubercular activity.

Diphenyl ether and derivatives can either activate or inhibit the aminopeptidase activity of leukotriene A_4 hydrolase, by binding at the hydrophobic pocket of LTA4H.



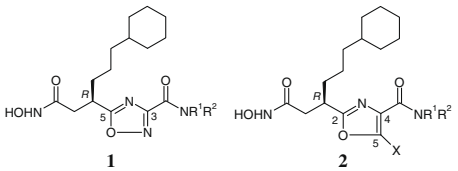


Forty caffeate analogues synthesized by one-pot methods were evaluated for their bioactivities. Four caffeate analogues possessed good HIV-IN inhibitory activities and several compounds showed good antitumor activities.



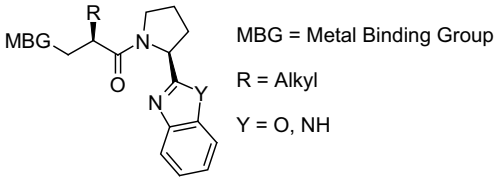
19

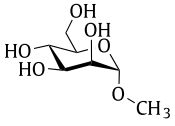
A series of new β-carboline derivatives, bearing a benzylidine substituent at position-1, has been prepared and evaluated in vitro against a panel of human cell lines. The N^2-benzylated β-carbolinium bromates represented the most interesting cytotoxic activities. Compounds **19** were found to be the most potent compounds with IC_{50} values lower than 5 μM against 10 strains human tumor cell lines.



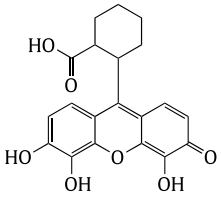
7: $NR^1R^2 = NH_2$

Succinyl hydroxamates **1** and **2** are disclosed as novel series of potent and selective inhibitors of procollagen C-proteinase which may have potential as anti-fibrotic agents. Carboxamide **7** was effective in a cell-based model of collagen deposition (fibroplasia model) and was very effective at penetrating human skin in vitro. Based on this profile, compound **7** (UK-383,367) was selected as a candidate for evaluation in clinical studies as a *topically* applied, dermal anti-scarring agent.

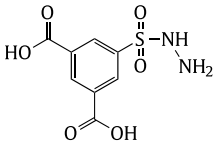




Methyl α-D-mannopyranoside
IC_{50} = 350μM



NSC 119910
IC_{50} = 29μM



NSC 120634
IC_{50} = 19μM

OTHER CONTENTS

*Corresponding author
Supplementary data available via ScienceDirect

COVER

Overlay of high resolution co-crystal structures of *R*-**22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5677.]

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