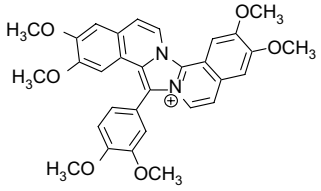
ELSEVIER

Bioorganic & Medicinal Chemistry Letters

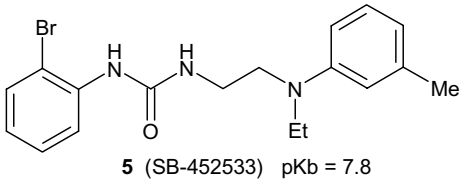
Bioorganic & Medicinal Chemistry Letters Vol. 14, No. 14, 2004

Contents

COMMUNICATIONS

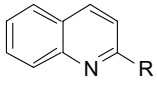


A new G-quadruplex selective ligand, fluorenylium derivative, binds preferentially with four-stranded DNA, it can bind weakly to the duplex and very weakly to ssDNA.

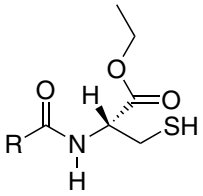


5 (SB-452533) pKb = 7.8

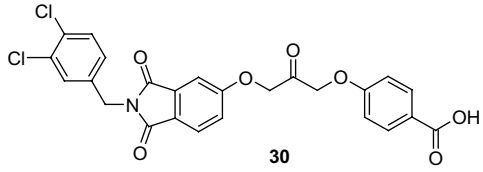
TRPV1 antagonist activity of **5** and the potential binding site of its quaternary salt is reported.



Several 2-substituted quinolines were synthesized and evaluated against several protozoa and against HTLV-1 transformed cells.

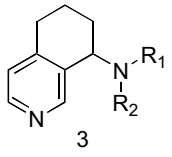


R-COOH: common NSAIDs



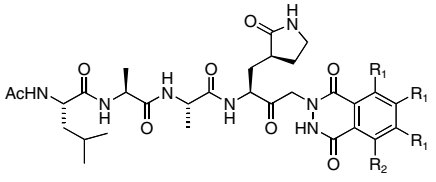
30

The high lipophilicity of a series of cytosolic phospholipase A_2 inhibitors has been reduced by the modification of a decyloxyphenyl chain designed to mimic the arachidonyl group of the natural substrate.



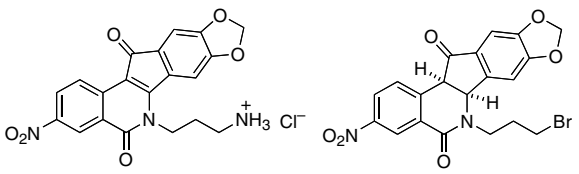
3

Several tetrahydroisoquinolines **3** were evaluated as novel nACh ligands. Although lacking significant affinity at nACh receptors, some (in particular **3** where $R_1 = Me$, $R_2 = Et$) displayed potent antinociceptive actions in a tail-flick assay.

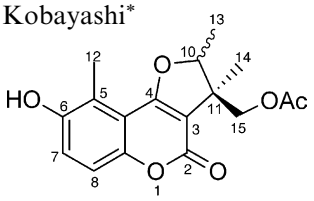


R_1 = H, F; R_2 = H, F, NO_2; IC_{50} = 1.6–2.5 μM

A series of keto-glutamine tetrapeptide analogs containing a 2-oxo-pyrrolidine ring as a glutamine side chain mimic were synthesized, which show improved inhibition against hepatitis A virus 3C proteinase.

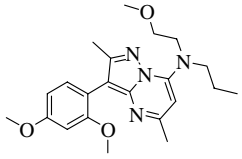


Substitution of the indenoisoquinoline system with an electron-withdrawing nitro group has been investigated as a strategy for increasing cytotoxicity and topoisomerase I inhibitory activity.



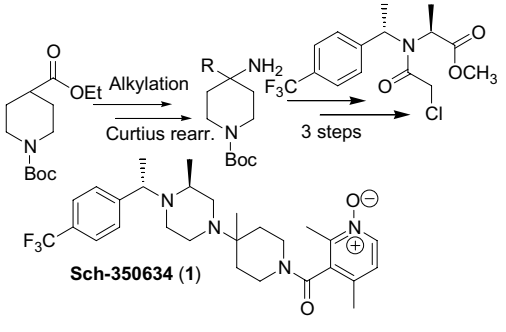
1: *10S11R*
2: *10R11R*

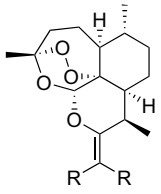
Two new coumarins, glaumacidines A (**1**) and B (**2**), and the related coumarins (**3**–**7**) have been isolated from the rhizomes of *Glaucidium palmatum* (Glaucidiaceae). The absolute configurations of **1** and **2** and *trans*- and *cis*-glaupadiols (**3** and **4**, respectively) were elucidated by spectroscopic data, chemical derivatization, and exciton chirality method. Glaupalol (**5**) enhanced the polymerization of tubulin and affected synergistically with paclitaxel on inhibition of KB cell proliferation.

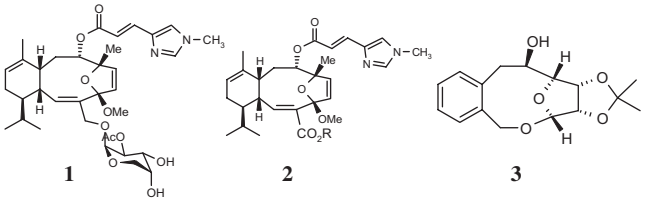


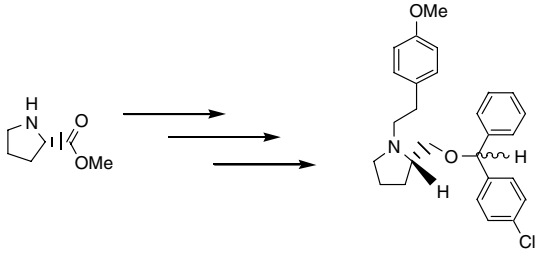
NBI 30545

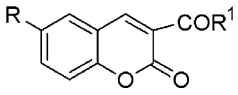
An efficient and convenient method for the synthesis of 4-differently substituted-4-aminopiperidine derivatives was described, employing isonipecotate as a starting material and Curtius rearrangement as a key step. With this key building block, we are able to efficiently synthesize piperazino-piperidine based CCR5 antagonist in a highly convergent manner free from toxic reagents such as diethylaluminum cyanide employed by previous procedures.

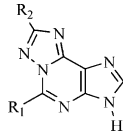






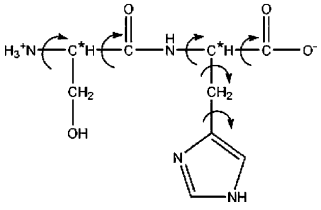




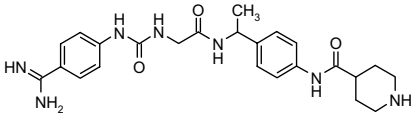


1-29

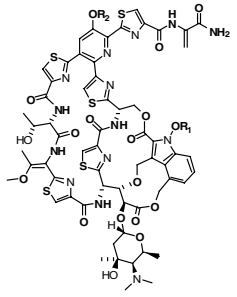
Considering potential of selective adenosine A_3 receptor antagonists in the development of prospective therapeutic agents, an attempt has been made to explore selectivity requirements of 1,2,4-triazolo[5,1-*i*]purine derivatives for binding with cloned human adenosine A_3 receptor subtype.



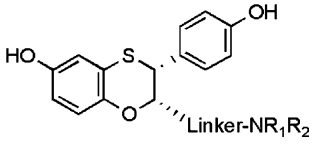
The key structural features for DNA cleaving activity were investigated.



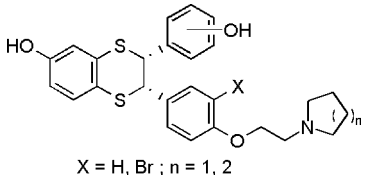
The amidinophenylurea scaffold was shown to provide an excellent template for the synthesis of novel and potent inhibitors of the blood coagulation factor VIIa. In this contribution we describe the structure-based design of potent ligands guided by X-ray crystallography, molecular modeling and docking studies. The design and synthetic efforts were directed towards novel modifications to explore the protease binding region close to the S4 subsite.



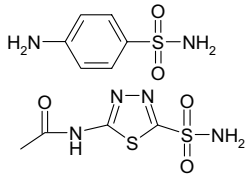
The synthesis and antibacterial activity of nocathiacin I analogues is described.

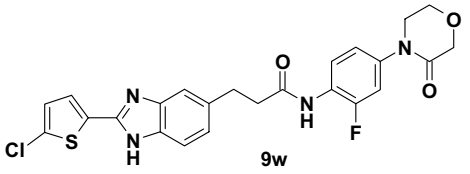


Modifications to the basic side chain region lead to a further understanding of the SAR of the dihydrobenzoxathiin class of SERAMs (Selective Estrogen Receptor Alpha Modulators).

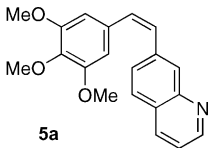


The synthesis and biological activity of dihydrobenzodithiins, as ERα-selective estrogen receptor ligands, are described.



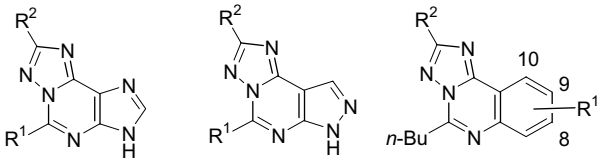


9w



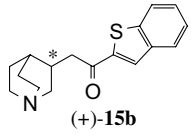
5a

The synthesis and biological evaluation of quinoline and quinoxaline analogues of combretastatin A-4 are described.



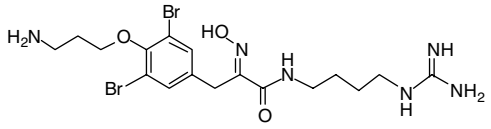
1 2 3

Structure–activity relationships (SAR) of fused 1,2,4-triazolo[1,5-*c*]pyrimidines (**1**, **2**, and **3**) were performed.

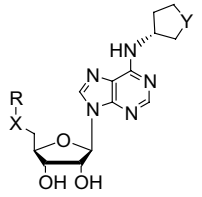


(+)-15b

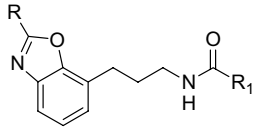
A series of 3-substituted 1-azabicyclo[2.2.2]octanes was discovered as the α7 nicotinic acetylcholine receptor agonists.



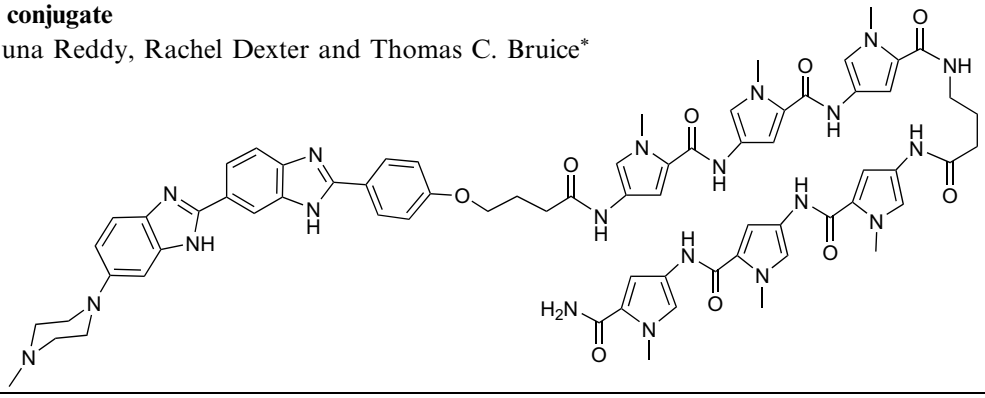
We first synthesized *N*-pentafluorobenzyl-1-deoxynojirimycin (5F-DNM), one new derivative of 1-deoxynojirimycin (DNM). It was found that 5F-DNM remarkably inhibited the secretion of IL-4 from human PBMCs and had a specific inhibition on the expression of CD4 molecules. 5F-DNM, much less toxic than cyclosporin A, might be used as a new candidate of immunosuppressant for specifically treating Th2-mediated immune diseases.

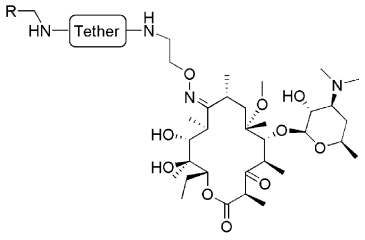


Potent partial A_1 AdoR agonists have been discovered.

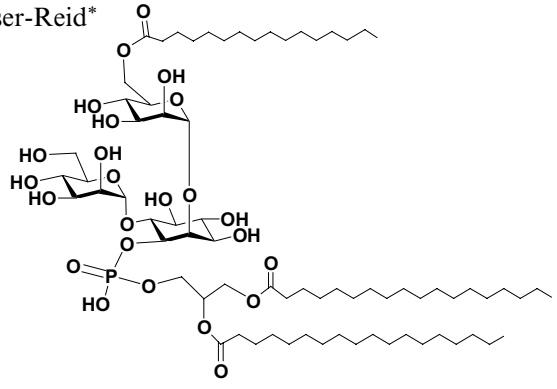


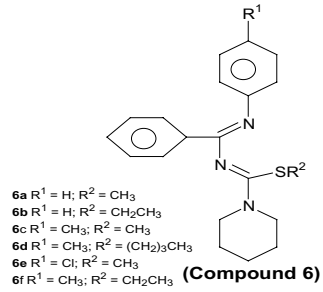
A series of benzoxazole derivatives was synthesized and evaluated as melatoninergic ligands. The binding affinity of these compounds for human MT_1 and MT_2 receptors was determined using 2-[^{125}I]-iodomelatonin as the radioligand. From this series of benzoxazole derivatives, compounds **14** and **17** were identified as melatonin receptor agonists.



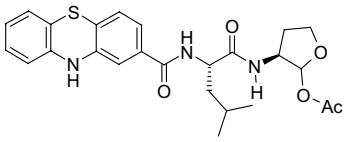


We report the discovery of a novel class of macrolide antibiotics that have improved antibacterial activity against Ery-resistant organisms.



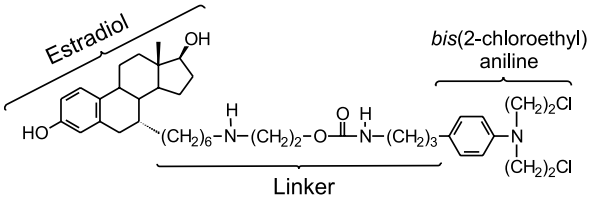


The synthesis and antimicrobial activity of amidine derived 1,3-diazabuta-1,3-diene derivatives are reported.

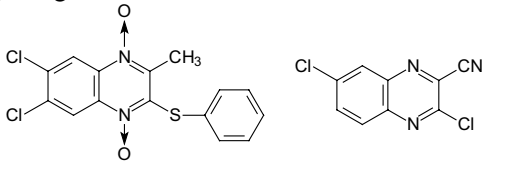


7

A series of hybrid compounds possessing calpain inhibitory and antioxidant properties has been synthesized. These compounds showed good inhibitory potencies in both activities. In addition, compound **7** provided effective protection against glial cell death induced by maitotoxin.



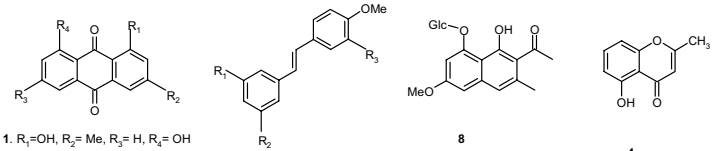
(1)



ID_{50}, Tulahuen, 6.5 μM
ID_{50}, Brener, 4.5 μM

ID_{50}, Tulahuen, 6.5 μM
ID_{50}, Brener, 4.5 μM

From our quinoxaline-library were identified new anti-chagasic leaders.



1. R_1=OH, R_2= Me, R_3= H, R_4= OH
2. R_1= OH, R_2= Me, R_3= OMe, R_4= OH
3. R_1= OH, R_2= Me, R_3= OH, R_4= OH
7. R_1= OH, R_2= Me, R_3= H, R_4= O-B-D-glucopyranoside

5. R_1= R_2= OH, R_3=H
6. R_1= R_2= R_3= OH
9. R_1=B-D-glucopyranoside R_2= OH, R_3= H

8

4

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 htBl (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htBl (center) allows for functional selection against thrombin (right) [Rajagopal, S.; Meza-Romero, R.; Ghosh, I. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1389].

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