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Bioorganic & Medicinal Chemistry Letters

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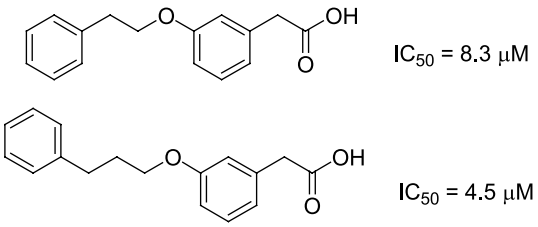
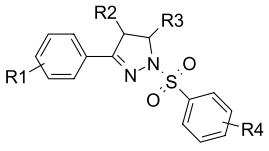
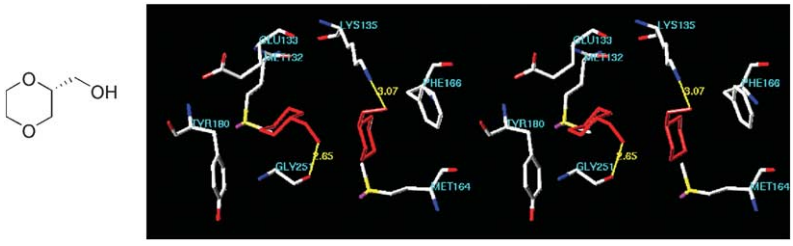
Contents

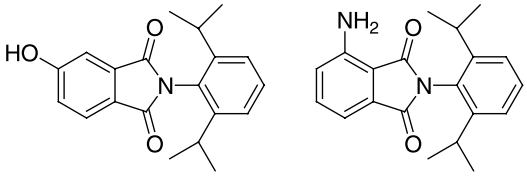
ARTICLES



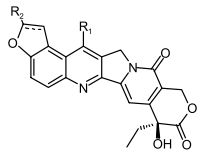




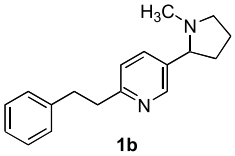
Dioxane-based antiviral agents targeted to the hydrophobic binding pocket of Sindbis virus capsid protein were designed by computer graphics molecular modeling and synthesized.



5HPP-33 4APP-33

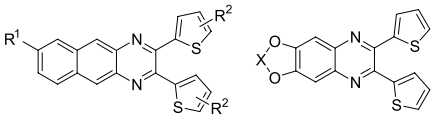


A series of hexacyclic camptothecins were synthesized and tested for antitumor activity in vitro and in vivo, and evaluated for the enzyme activity of inhibiting the topoisomerase I and the stability of the lactone ring.



1b

Defying presumed structure–affinity relationships, nicotine analog **1b** (K_i = 15 nM) was unexpectedly found to bind to α4β2 nACh receptors. Administered via an intrathecal route, **1b** antagonized the antinociceptive actions of (−)nicotine in the mouse tail-flick assay.

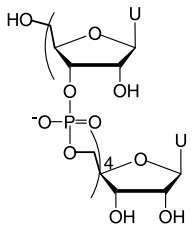


R^1 = carboxylic acid, H
R^2 = alkyl-carboxylic acid, H

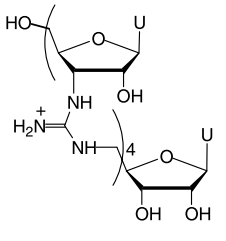
X= $(CH_2)_n$
n= 1-3

A series of novel tricyclic quinoxaline derivatives was prepared and examined on SRPK-1 kinase assay and on a selectivity panel of 19 kinase assays.

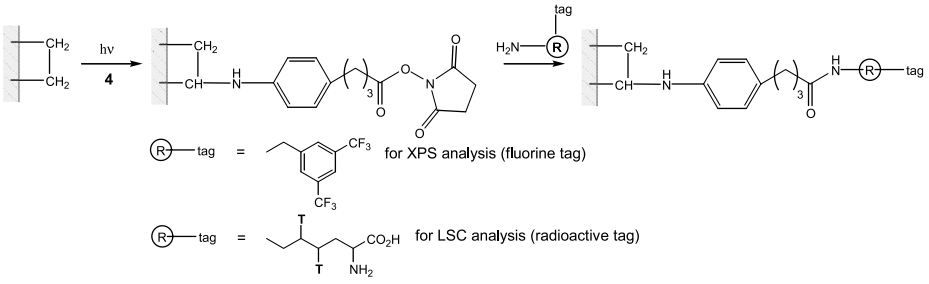
Replacement of the phosphodiester linkages of the polyanionic uridyl RNA with guanidium linkers provides polycationic uridyl ribonucleic guanidine (RNG) as a putative antisense/antigene agent. DNA binding characteristics of cationic uridyl RNG are described.

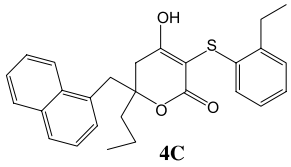


RNA



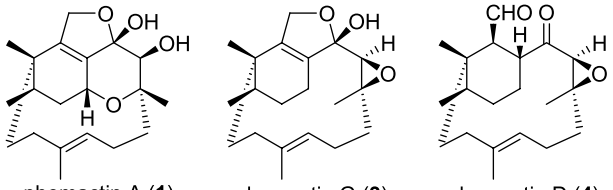
RNG





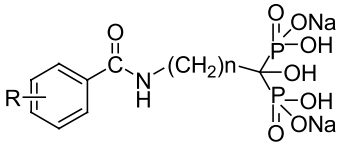
4C

Synthesis and biological evaluation of 24 4-hydroxypyrone derivatives are described. Compound **4C** was the most potent inhibitor in this study, with an EC_{50} value at 1.7 μM and a therapeutic index of 46.



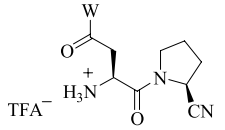
phomactin A (**1**) phomactin G (**3**) phomactin D (**4**)

A range of natural and unnatural phomactins, recently synthesised in our laboratory, were found to exhibit PAF antagonism with pIC_{50} values in the range of 5.6–6.2.

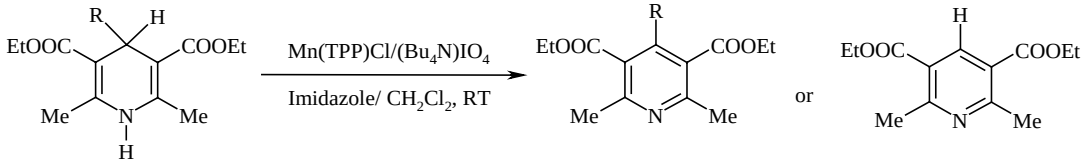


3

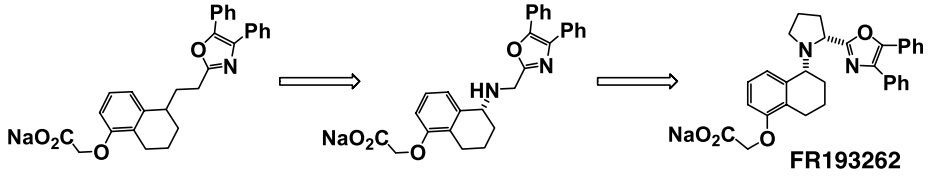
A novel series of bisphosphonates with activities both on bone resorption and formation have been synthesized.

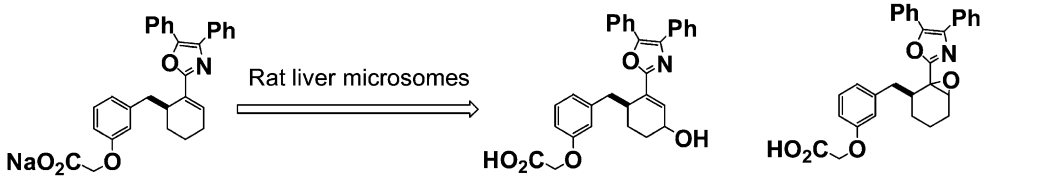


W=1,2,3,4-tetrahydroisoquinolin derivatives
W=piperazine derivatives
W=benzylamine derivatives
W=phenethylamine derivatives



Efficient oxidation of Hantzsch 1,4-dihydropyridines to their corresponding pyridine derivatives with $(Bu_4N)IO_4$ catalyzed by tetraphenylporphyrinatomanganese(III) chloride, [Mn(TPP)Cl], is reported.

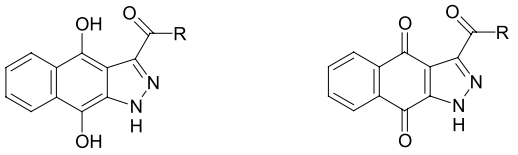




1

M-1: α-OH or β-OH
M-2: β-OH or α-OH

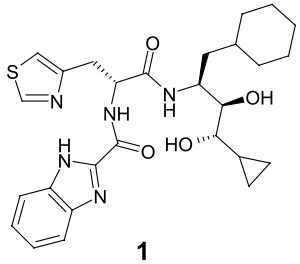
M-4
(mixture of α and β-epoxide)



2-5 R=OEt, NH-R^1, NH-NH-R^2 **3-7**

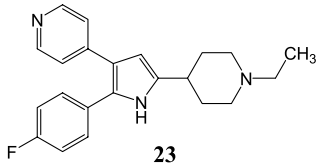
A series of (1,4)-naphthoquinono [3,2-*c*]-1*H*-pyrazoles and their (1,4)-naphthohydroquinone derivatives **2**–**7** were synthesized and evaluated for antifungal, antibacterial, and anticancer activities.

We report the discovery, gram scale synthesis and binding results for compound **1**, the first potent, drug-like selective $P2X_1$ receptor antagonist described. Compound **1** was shown to be more than 30-fold selective over other purinergic receptor subtypes.

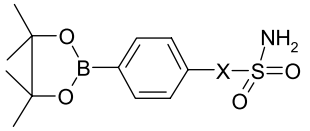


1

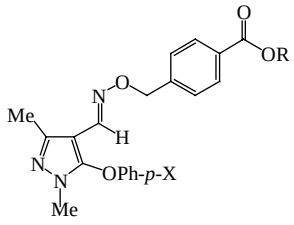
Several analogs of 2,3-diaryl pyrroles were synthesized and evaluated as inhibitors of *Eimeria tenella* cGMP-dependent protein kinase and in in vivo anticoccidial assays. The *N*-ethyl analog 23 was chosen for a field trial as a novel anticoccidial agent.



23



X = NH, O, or nothing



R = Et, Bu^t; X = H, Cl

A series of pyrazole oxime ether derivatives were prepared and examined as cytotoxic agents. In particular, 5-phenoxypyrazole was comparable to doxorubicin, while exhibiting very potent cytotoxicity against XF 498 and HCT15.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Ameliorating transthyretin amyloidogenesis by native state kinetic stabilization mediated by small molecule binding. Small molecule binding to the amyloidogenic protein transthyretin kinetically stabilizes the native tetrameric state, preventing dissociation to folded monomers that misfold and misassemble into toxic intermediates, amorphous aggregates, and amyloid fibrils. The Kelly laboratory has developed several structurally distinct inhibitor families, depicted in the background, that are undergoing pharmacological evaluation. Created by Steven M. Johnson, graduate student in Professor Jeffery W. Kelly's laboratory, Department of Chemistry, The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA.

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

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