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Bioorganic & Medicinal Chemistry Letters

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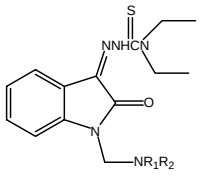
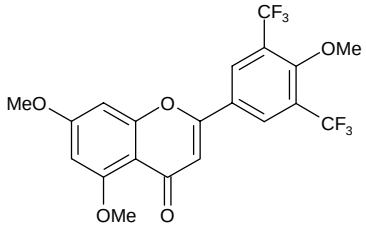
Contents

ARTICLES

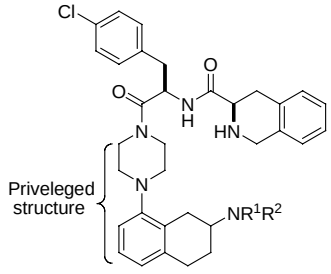


1-9

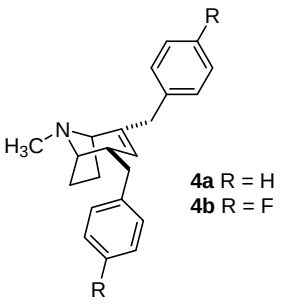
A series of isatin β-thiosemicarbazones derivatives was synthesized and evaluated for anti-HIV activity in HTLV-III_B strain in CEM cell line. Compound **6** was found to be the most active compound with an EC_{50} value of 2.62 μM.

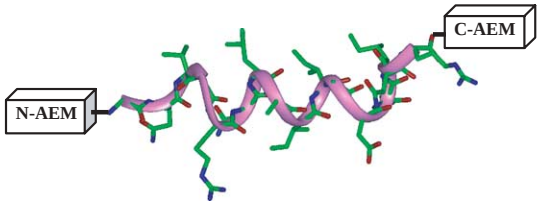


Tetrahydroquinolines, indoles, and aminotetralines provide useful privileged structures for the construction of ligands with affinity for melanocortin 4 receptors.



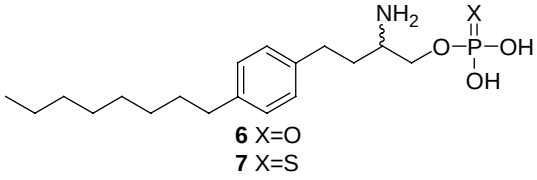
A series of tropane derivatives has been synthesized as lobelane analogues and evaluated for their binding affinity at the vesicular monoamine transporter-2 (VMAT2), and at α4β2* and α7* nicotinic acetylcholine receptors. The trop-2-ene analogues **4a** and **4b** exhibited good affinity and high selectivity for VMAT2.



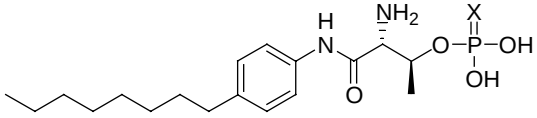


A new strategy for studying and mimicking helical peptide–protein interactions involved in apoptosis.

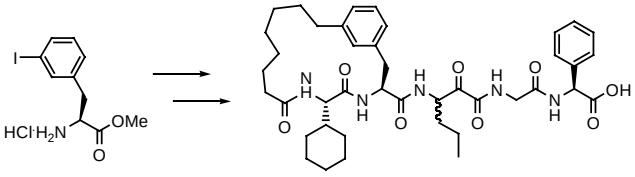
The synthesis and biological activity of phosphothioates, as subtype selective sphingosine-1-phosphate receptor agonists, are described. Sphingosine-1-phosphate receptor agonist **12** is degraded to its alcohol in vivo. Compared to their phosphate precursors, phosphothioate compounds **7** and **13** were shown to induce lymphopenia for protracted intervals in vivo.



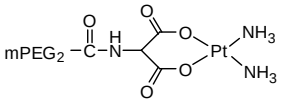
6 X=O
7 X=S



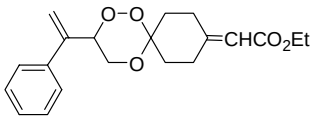
12 X=O
13 X=S



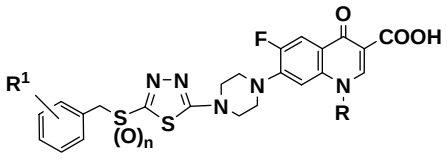
HCV NS3 protease inhibitor



Two-arm branched mPEG was synthesized and used as carrier for immobilization of CDDP.

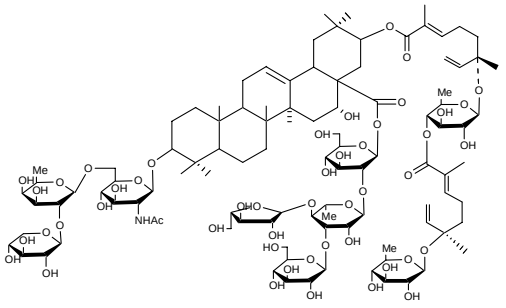


A series of *N*-(5-benzylthio-1,3,4-thiadiazol-2-yl) and *N*-(5-benzylsulfonyl-1,3,4-thiadiazol-2-yl) derivatives of piperazinyl quinolones was synthesized and evaluated for antibacterial activity. Some of these derivatives exhibit comparable or more potent activity against Gram-positive bacteria; *Staphylococcus aureus* and *Staphylococcus epidermidis*, with respect to the reference drugs. The SAR of this series indicates that both the structure of the benzyl unit and the S or SO_2 linker dramatically impact antibacterial activity.

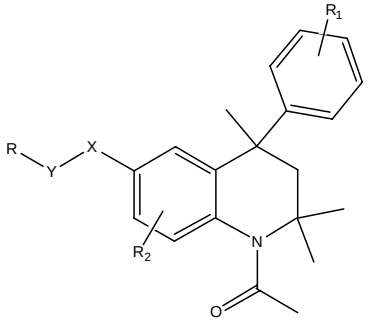


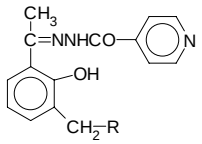
R= ethyl, cyclopropyl
R^1 = H, NO_2
n= 0, 2

The structure of a new triterpenoid saponin julibroside J_{28}, isolated from *Albizia julibrissin*, has been determined on the basis of comprehensive spectroscopic analysis. Julibroside J_{28} had marked antitumor activity.



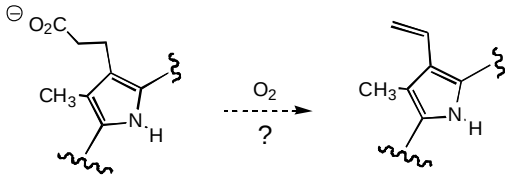
QSAR analysis on recently reported 6-amino-4-phenyltetrahydroquinoline derivatives as FSH receptor antagonists has been presented.



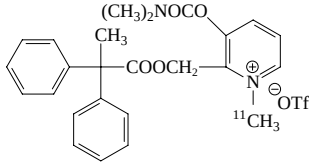


1-15

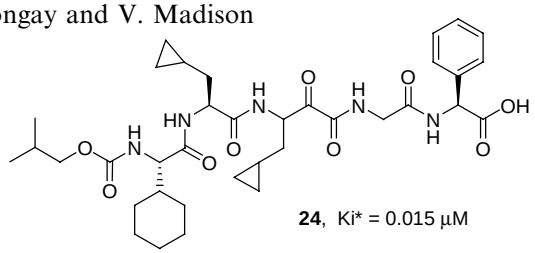
2-Hydroxy acetophenone react with isoniazid to form acid hydrazones. The C-Mannich bases of the above acid hydrazone were prepared by reacting them with formaldehyde and various secondary amines. Compound *N*′-{1-[2-hydroxy-3-(piperazin-1-ylmethyl)phenyl]ethylidene}isonicotinohydrazide **8** was found to be the most active compound with MIC of 0.56 μM/mL and was more potent than isoniazide (MIC of 2.04 μM/mL).



A new mechanism is proposed to explain how coproporphyrinogen oxidase performs two oxidative decarboxylations on a porphyrinogen substrate without the aid of cofactors or metal ions in the presence of molecular oxygen.

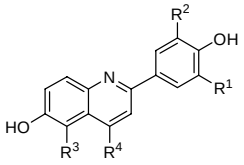


[^{11}C]MDDP, [^{11}C]**1**

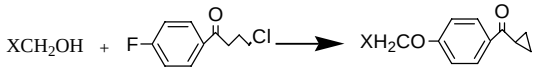


24, Ki* = 0.015 μM

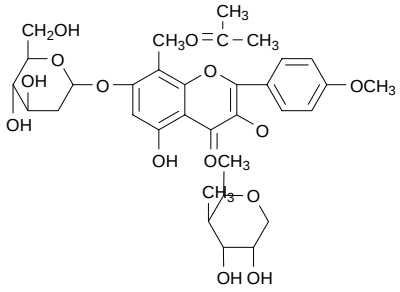
Modification of the P_2 and P_1 side chains of earlier P_3-capped α-ketoamide inhibitor of HCV NS3 serine protease **1** resulted in the discovery of compound **24** with about 10-fold improvement in potency.



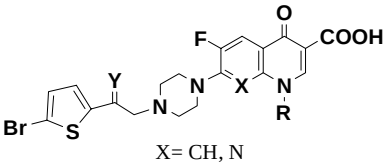
A series of 2-phenylquinoline derivatives was prepared and displayed high affinity and significant selectivity for estrogen receptor β.



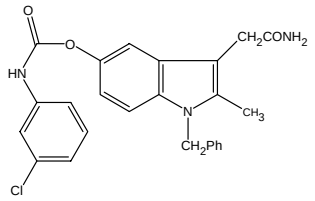
Aryloxy phenyl cyclopropyl methanones were synthesized and evaluated as new potent anti-tubercular agents.



A series of *N*-[2-(5-bromothiophen-2-yl)-2-oxoethyl] and *N*-[2-(5-bromothiophen-2-yl)-2-oximinoethyl] derivatives of piperazinyl quinolones were synthesized and evaluated for antimicrobial activity. Some of these derivatives exhibit comparable or better activity against Gram-positive bacteria, than ciprofloxacin, norfloxacin and enoxacine as reference drugs.



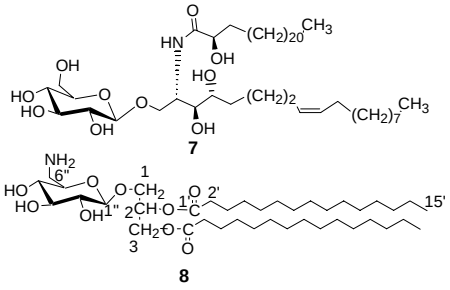
X= CH, N
Y= O, NOH, NOBn
R= cyclopropyl, ethyl



5

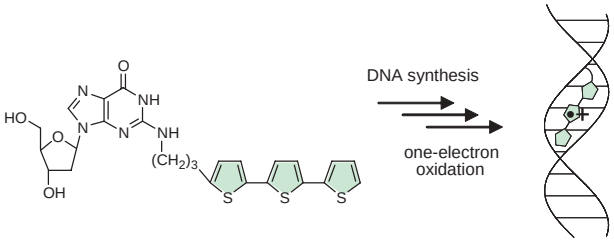
The synthesis of the human non-pancreatic secretory phospholipase A2 inhibitor (IC_{50} = 1.81 ± 0.59 μM) is reported.

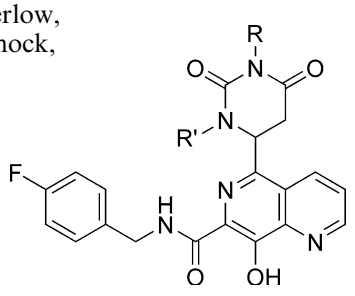
Two glycolipids were identified from *Desmodium gangeticum* to possess antileishmanial and immunomodulatory activities. Aminoglucosylglycerolipid (**8**) was found to be novel.

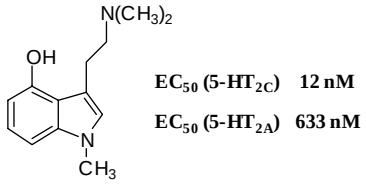


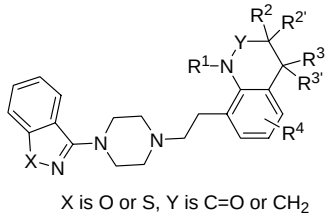
7

8

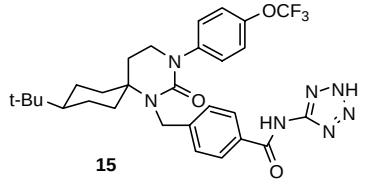








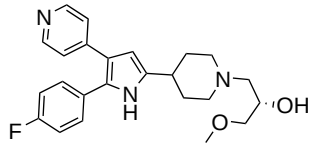
The synthesis and biological activity of novel 8-substituted 3,4-dihydroquinolinones, tetrahydroquinolines, and *N*-acyltetrahydroquinolines are disclosed.



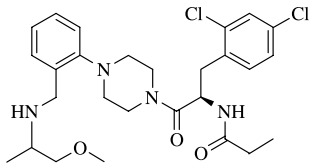
15

The discovery and SAR study of a novel spiro-urea series of human glucagon receptor antagonists such as **15** are presented.

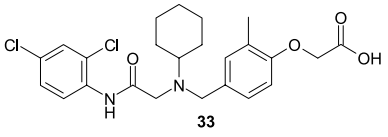
Diaryl-(4-piperidinyl)-pyrrole derivatives bearing hydroxylated *N*-alkyl substituents have been synthesized and evaluated as anticoccidial agents.



4b IC_{50} = 0.56 nM



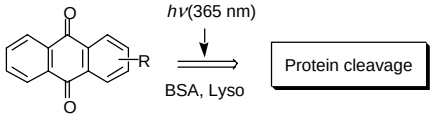
7b

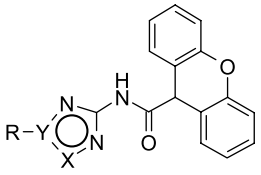


33

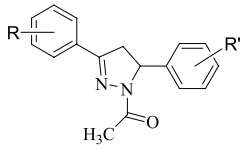
*h*PPARδ 0.003 μM

We report the solid-phase synthesis and pharmacological evaluation of a new series of small-molecule agonists of the human peroxisome proliferator-activated receptor δ (PPARδ) based on a lead structure from our PPARα program. Compound **33** showed good pharmacokinetics.





Small molecule mGluR1 enhancers **3** (X = O, Y = C) and **4** (X = Y = N) were synthesized as pharmacological tools for the study of the physiological roles mediated by mGlu1 receptors.



A series of substituted pyrazoline were synthesized and evaluated for their anticancer activity and for their ability to inhibit P-glycoprotein-mediated multidrug resistance.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Amerliorating 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.

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