ELSEVIER

Bioorganic & Medicinal Chemistry Letters

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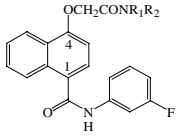
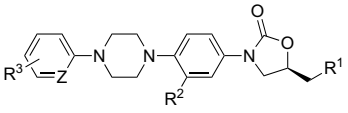
Contents

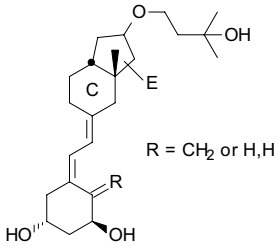
COMMUNICATIONS



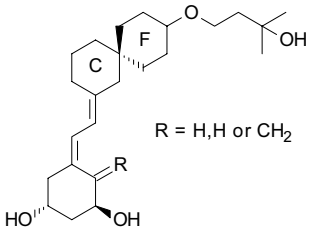
Structure-based-design studies, based upon the crystal structure of the HOXB1–PBX1/DNA transcription factor complex, were used to identify 1,4-disubstituted naphthalenes as selective antagonists that block the formation of this complex, as well as related complexes.



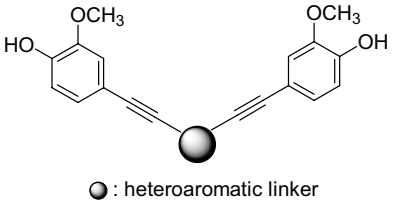
R^1 = O-2-Pyridine, R^2 = F, R^3= 2-Cl, Z = H
R^1 = O-2-Pyrazine, R^2 = F, R^3= 2-Cl, Z = H
R^1 = O-2-Isoxazole, R^2 = F, R^3= 2-Cl, Z = H
R^1 = N(C=S)CH_3, R^2 = F, R^3= various substituents, Z = H or N
R^1 = N(C=S)SCH_3, R^2 = H or F, R^3= various substituents, Z = H or N
R^1 = N(C=S)NH_2, R^2 = H or F, R^3= various substituents, Z = H or N
R^1 = N(C=S)OCH_3, R^2 = F, R^3= various substituents, Z = H or N

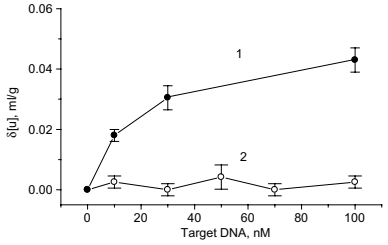


The synthesis and biological activity of novel CE-ring 22-oxa-1α,25$(OH)_2D_3$ analogues is described.

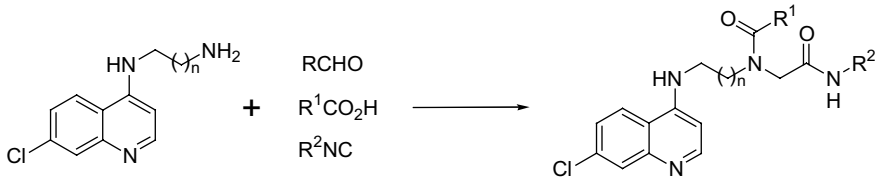


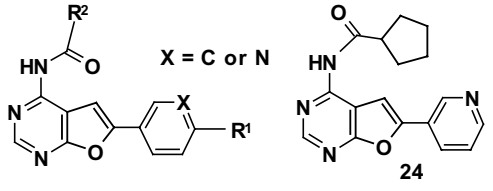
The synthesis and biological activity of novel CF-ring 22-oxa-1α,25$(OH)_2D_3$ analogues is described.



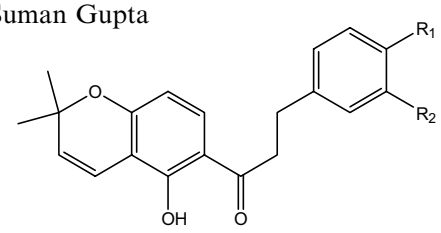


DNA hybridization on a liposome surface resulted in increase of ultrasound velocity increment [*u*] (1). No changes were observed following addition of noncomplementary chain (2). These changes are due to liposome aggregation.

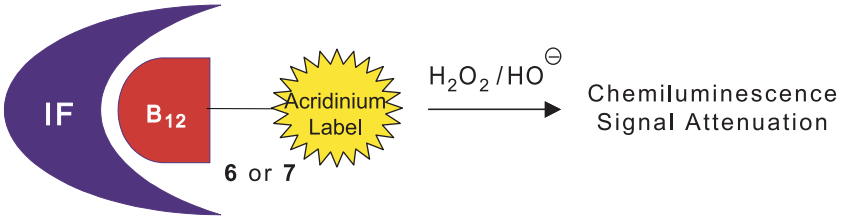


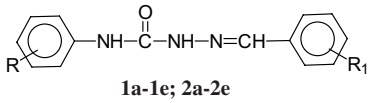


A novel and potent series of selective GSK-3 inhibitors are described. Some derivatives showed excellent potency in a cellular assay.



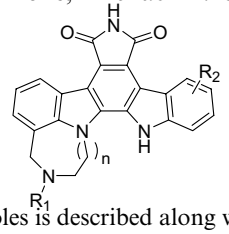
Chromeno dihydrochalcones contain a 2′,2′-dimethyl benzopyran system, which are frequently encountered in many natural products and exhibit a variety of biological activities. We report the convenient route for the synthesis of chromeno dihydrochalcones and in vitro antileishmanial activity of chromeno dihydrochalcones and their intermediates.



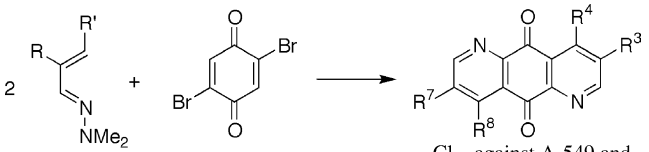


1a-1e; 2a-2e

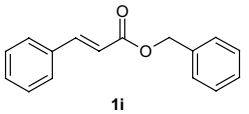
During the course of our work on the synthesis and screening of new drugs for tuberculosis, we have identified N1-(4-acetamido phenyl)-N4-(2-nitro benzylidene) semicarbazone (**1b**), which inhibited in vitro *Mycobacterium tuberculosis* $H_{37}Rv$; 100% inhibition at 1.25 μg/mL.



The synthesis of a novel series of aza-1,7-annulated indoles is described along with their conversion to indolocarbazoles that proved to be potent kinase inhibitors.

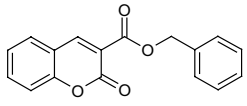


Cl_{50} against A-549 and MEL-28 up to 10^{-8} M



1i

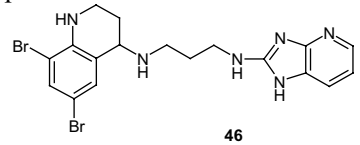
IC_{50} = 0.7 μM (oxidation)
IC_{50} = 7 μM (reduction)



2a

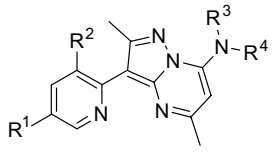
IC_{50} = 2.7 μM (oxidation)
IC_{50} = 8 μM (reduction)

A series of cinnamates and coumarin-3-carboxylates was synthesized and evaluated for inhibition of 17β-hydroxysteroid dehydrogenase from the fungus *Cochliobolus lunatus*.

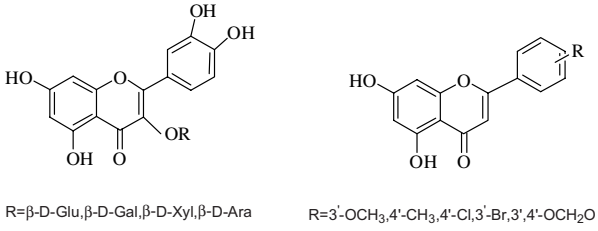


46

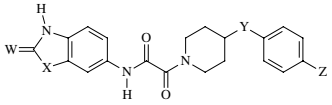
The right hand side pharmacophore for potent MRS inhibition has been defined as an NH–C–NH functionality in the context of a heteroaromatic bicycle. Potent antibacterial active fused-pyrimidone and fused-imidazole analogues have been obtained and enantioselective activity demonstrated. Compound **46** demonstrated very good antibacterial activity against panels of antibiotic-resistant staphylococci and enterococci.



15-21

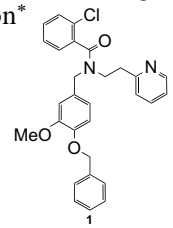


Several 5,7-dihydroxyflavone and quercetin 3-*O*-glycosides have been synthesized and evaluated for vasorelaxant activity. A log *P*–activity relationship amongst flavonoids was suggested.



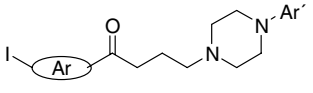
A

Compounds of general formula **A** with potent p.o. analgesic activity were prepared. W=O or S; X=O, S, NH, CH_2, CH_2O or OCH_2; Y=CH_2 or O; Z=H, F, Cl or CH_3.

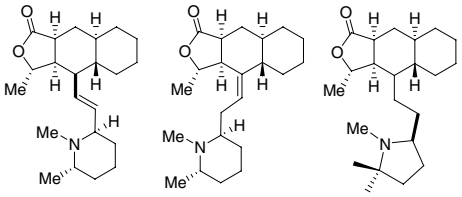


1

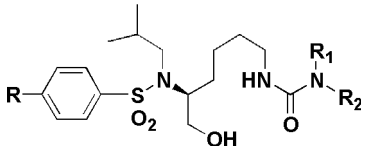
Structurally conservative modifications of a Ras/Raf protein interaction inhibitor were rapidly effected utilizing solution phase parallel synthesis in order to generate preliminary structure–activity relationship information vis-à-vis inhibition of the MAPK pathway.



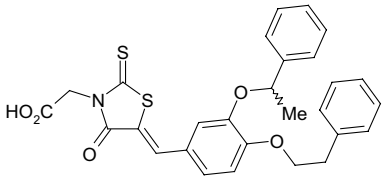
Highly selective dopamine D3 receptor radioligands were synthesized. The benzofuran derivative **11b** displayed D3 selectivity of 560-fold over D2 (K_i 5.7 nM) justifying an application as a SPET radioligand.



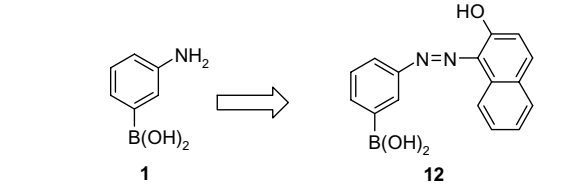
A number of analogs of the natural product himbacine were synthesized employing variations at the heterocyclic unit and the tether that links the heterocyclic unit to the tricyclic motif. Several of these analogs had M_2 affinity and M_1/M_2 selectivity comparable to those of himbacine.



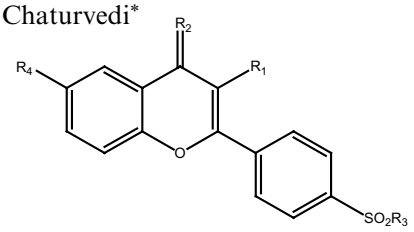
A series of *N*α-isobutyl-*N*α-arylsulfonamido-(*N*ε-ureas) lysine and lysinol derivatives were prepared and evaluated as inhibitors of HIV protease and wild type virus.



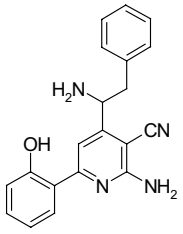
Inhibitors of fungal protein: mannosyl transferase 1 (PMT1) are described, which inhibit *Candida albicans* PMT1 with IC_{50}s in the range 0.2–0.5 μM. Members of the series are effective in inducing changes in morphology of *C. albicans* in vitro that have previously been associated with loss of the transferase activity.



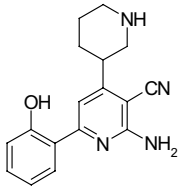
The synthesis and biological evaluation of aza-boronic derivatives are reported.



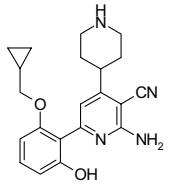
A series of recently reported novel selective cyclooxygenase-2 inhibitors was subjected to quantitative structure–activity relationship (QSAR) analysis. Our investigations discerned important structural insights apropos of R_1, R_2, R_3, and R_4 modifications to abet the design of potent COX-2 inhibitors among these congeners.



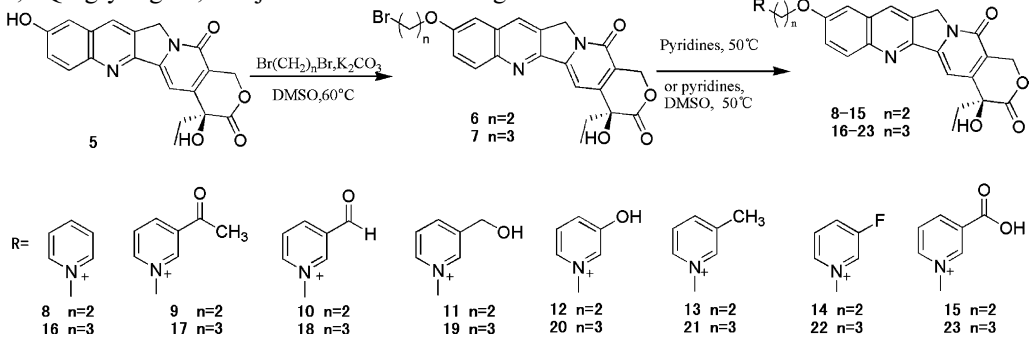
IC_{50} = 60 nM (IKK-β)
IC_{50} = 8000 nM (Cell)

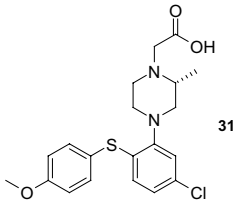


IC_{50} = 25 nM (IKK-β)
IC_{50} = 300 nM (Cell)



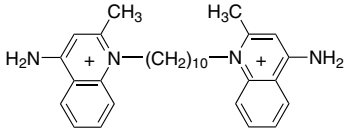
IC_{50} = 8.5 nM (IKK-β)
IC_{50} = 40 nM (RANTES/Cell)





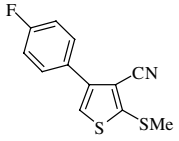
31

A novel series of GlyT-1 inhibitors are described. The most potent compound, 31 was demonstrated to elevate glycine levels in the rat ventral hippocampus as measured with microdialysis.



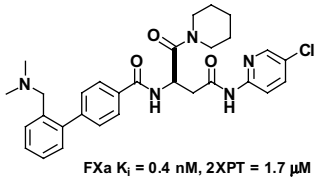
Dequalinium

$pIC_{50} = 0.086(\pm0.011)\ \alpha + 2.06(\pm0.28)$
$n=20,\ r=0.89,\ r^2=0.79,\ s=0.522,\ F=66.48$



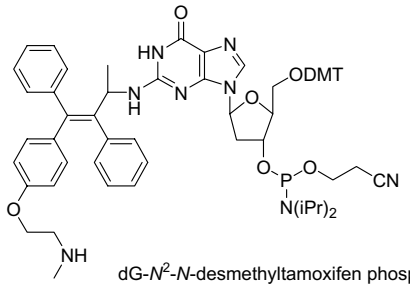
1

A new series of analogues of 4-(4-fluorophenyl)-2-methylthio-thiophene-3-carbonitrile (**1**) were synthesized and evaluated for their in vitro and in vivo anthelmintic activity against *Haemonchus contortus*.

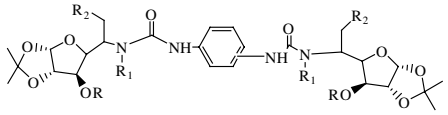


FXa K_i = 0.4 nM, 2XPT = 1.7 μM

Parallel synthesis and iterative optimization led to the discovery of a series of inhibitors having excellent in vitro and promising in vivo properties.



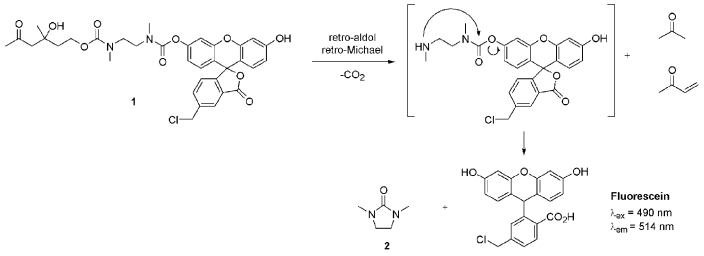
dG-N^2-*N*-desmethyltamoxifen phosphoramidite derivative



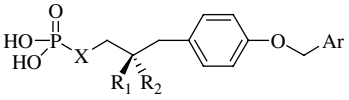
A series of phenylene bridged C_2 symmetric glycosyl ureides were synthesised and evaluated against *Leishmania donovani* and two of them reduced the dose of standard drug SSG.

Acute liver injury caused by D-galactosamine⟶Increase in plasma ceramides with a long acyl chain.

The concentration of major ceramides (C24:0, C24:1, C16:0, C22:0, C22:1, and C18:0) in plasma increased 24 h after administration of D-galactosamine and the total ceramide concentration was also increased to 3.6 times that in the control. In the liver, minor ceramide components were increased by this toxin.

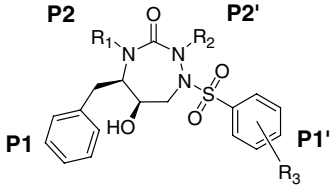


High-throughput screening of cells expressing active catalytic antibody clones by flow cytometry using a designed fluorogenic retro-aldol retro-Michael substrate is described.

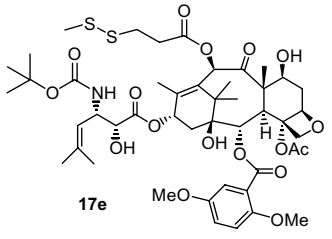


1: $R_1 = NHC(O)C_{17}H_{33}$; $R_2 = H$; Ar = 2-pyr; X = O
LPA_1: K_i = 18 nM; LPA_3: IC_{50} = 175 nM
13d: $R_1 = NHC(O)C_{17}H_{33}$; $R_2 = H$; Ar = 2-(4-OMe-3,5-diMe-pyr); X = CH_2
LPA_1: IC_{50} = >10000 nM; LPA_3: IC_{50} = 150 nM

A recently reported dual LPA_1/LPA_3 receptor antagonist (**1**) has been modified so as to modulate the basicity, sterics, and dipole moment of the 2-pyridyl moiety. This study has resulted in the development of the first nonhydrolyzable and presumably phosphatase-resistant LPA_3-selective antagonist (**13d**) reported to date.

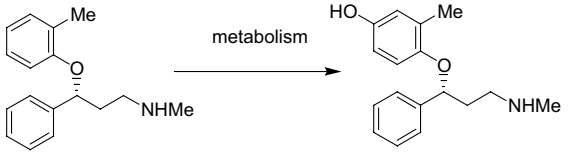


A novel series of P1′ arylsulfonamide azacyclic ureas were prepared and evaluated as inhibitors of HIV protease. The X-ray crystal structure of an analog bound in the enzyme active site is presented.

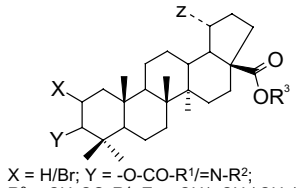


17e

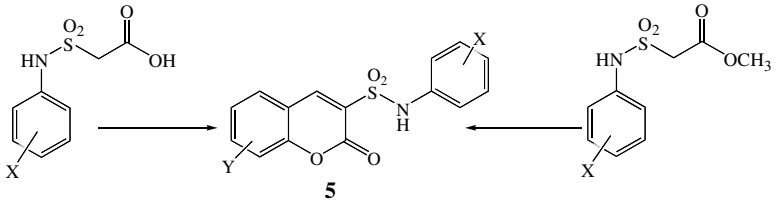
Synthesis and biological evaluation of the major metabolite of atomoxetine: elucidation of a partial κ-opioid agonist effect **pp 4083–4085**
Christopher J. Creighton,* Kris Ramabadran, Patrick E. Ciccone, Jingchun Liu, Michael J. Orsini and Allen B. Reitz*



Atomoxetine **4-Hydroxyatomoxetine**

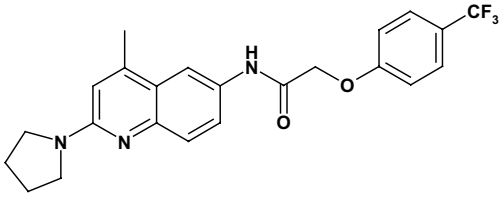


X = H/Br; Y = -O-CO-R^1/=N-R^2; R^3 = $CH_2CO_2R^4$; Z = -CH(=CH_2)CH_3/ -$CH(CH_3)_2$/C(Br)(CH_2Br)CH_3

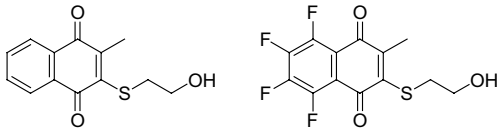


5

Synthesis of novel coumarin-3-sulfonamides and their ability to activate JNK1 and kill cancer cells in vitro is described.

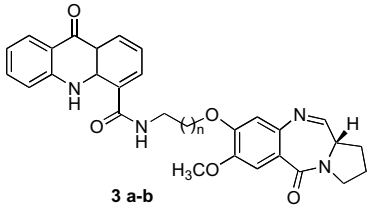


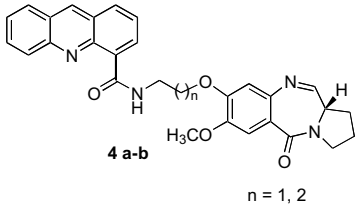
Structure–activity relationships of 2-aminoquinolines as MCH-1R antagonists are reported.



Cpd 5 **Fluorinated-Cpd 5**

We report on the fluorinated form of Cpd 5 as a cell growth inhibitor.





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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