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Bioorganic & Medicinal Chemistry Letters

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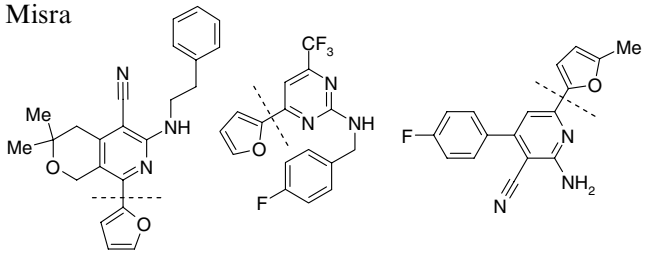
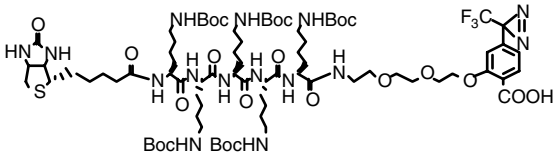
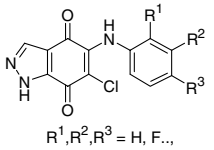
Contents

ARTICLES



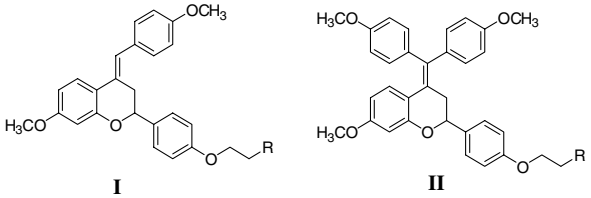
Identification of potent, non-furan containing A_{2A} antagonists using database mining.



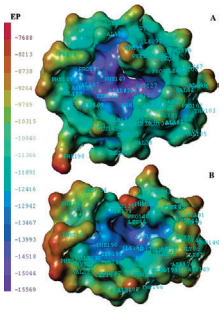


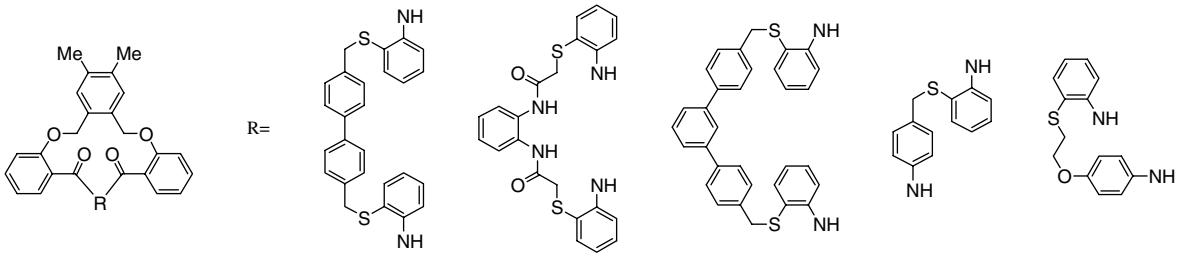
R^1, R^2, R^3 = H, F..,

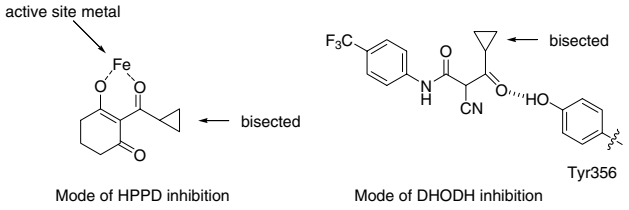
5-Arylamino-6-chloro-1*H*-indazole-4,7-diones were synthesized and evaluated for their inhibitory activity on protein kinase B/AKT. The 5-arylamino-6-chloro-1*H*-indazole-4,7-diones exhibited a potent Akt1 inhibitory activity.

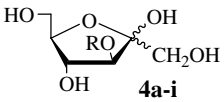


I **II**



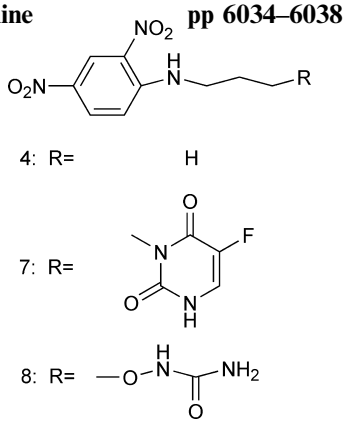


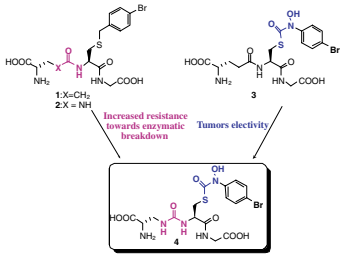


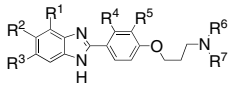


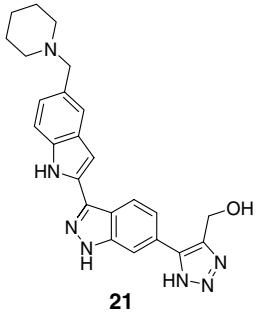
4a-i

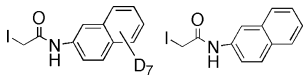
R = D-Galp, D-Manp, L-Rhap, D-Arap, D-Xylp, D-Ribp, D-lactose, D-cellobiose, D-maltose.





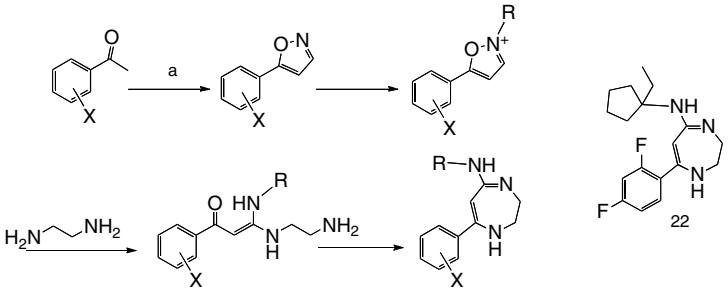


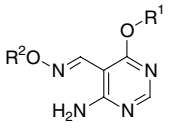




D-labeled and unlabeled *N*-β-naphthyliodoacetamides that covalently react with cysteine residues have been synthesized and applied to quantitative analysis of peptides.

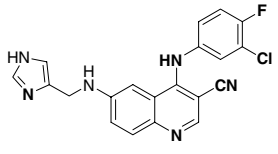
A several series of low molecular weight 5-HT$_{2A}$ leads were identified from an analysis of HTS data, the exploration of SAR and optimisation one series using parallel synthesis is described affording compound **22** (5-HT$_{2A}$ IC$_{50}$ 1.1 nM).

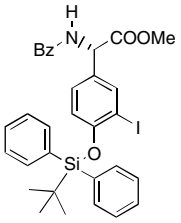




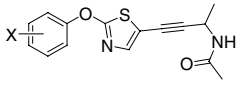
A novel 4-aminopyrimidine-5-carboxaldehyde oxime scaffold with inhibitory activity against VEGFR-2 kinase has been identified. With a 4-fluoro-2-methylindol-5-yloxy group at the 6-position and alkyl groups as the oxime side chains, many analogues showed good potency for VEGFR-2. This series also exhibited antiproliferative activity against cancer cells, causing cell accumulation at the G2/M phase of the cell cycle and preventing cells from entering mitosis.

The synthesis and structure–activity studies of a series of quinoline-3-carbonitriles as inhibitors of Tpl2 kinase are described. Potent inhibitors of Tpl2 kinase with selectivity against a panel of selected kinases in enzymatic assays and specificity in cell-based phosphorylation assays in LPS-treated human monocytes were identified. Selected inhibitors with moderate activity in human whole blood assay effectively inhibited LPS/D-Gal induced TNFα release when administered intraperitoneally in mice.

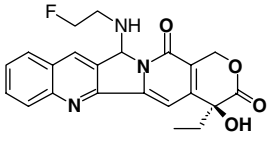




The discovery and synthesis of genotoxic (haloaryl)glycines is reported.

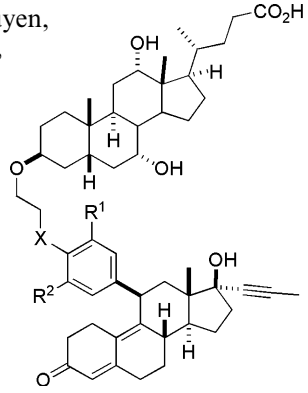


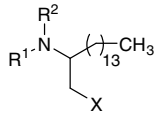
The SAR for a novel series of acetyl-CoA carboxylase inhibitors are described. Optimization of distal aryl ring substitution in the lead scaffold resulted in the identification of compounds displaying low-nanomolar potency and high isozyme-selectivity for acetyl-CoA carboxylase 2.



A series of 5-aminosubstituted camptothecin analogs were prepared using microwave accelerated synthesis. A fluoroethyl derivative showed superior inhibitory activity to camptothecin against the hypoxia inducible factor HIF-1α.

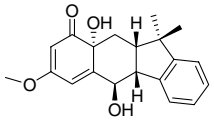
A series of potent steroidal glucocorticoid receptor antagonists has been discovered. After conjugation to cholic acid, the compounds retained an affinity for GR in vitro and had modest in vivo efficacy.



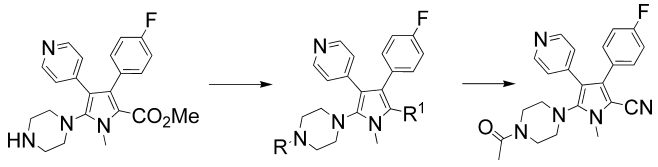


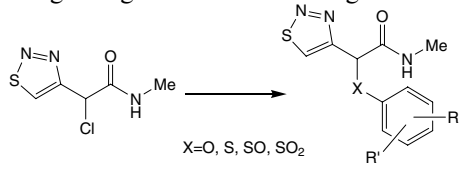
X: OH, OBn, NR^1R^2
R^1, **R^2**: H, Alkyl, Boc, glutaryl

Lymphoproliferation inhibition and delayed hypersensibility assays have served to select primarily the compounds to be evaluated further, through Graft-*vs*-Host reaction, NO production and other assays, in order to determine the potential of the title compounds for being used as immunomodulators.

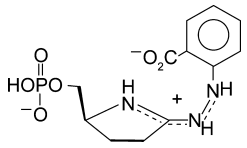


The elucidation and the antioxidant activities of a new prenyl stilbenoid are reported.

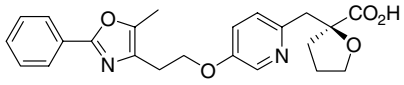




A series of α-substituted-1,2,3-thiadiazoleacetamides were prepared and tested in vitro against tobacco mosaic virus. The preliminary bioassays indicated that some of the new compounds are good as compared to the commercial pesticide Virus A at 500 mg/L, and the activity was influenced by the nature of the substituents. 3D-QSAR models were established based on the antiviral activity of the compounds. It has also been found that some of the new compounds also exhibit significant anti-HBV activity in human hepatoblastoma-derived liver Hep-G2 cells.



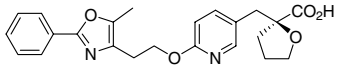
A mimic of the putative transition-state intermediate has been synthesized and found to be a very slow-onset inhibitor of yeast orotate phosphoribosyltransferase. The mechanism of inhibition may involve a rate-determining isomerization of the enzyme to a form receptive to the inhibitor, which then remains tightly bound.



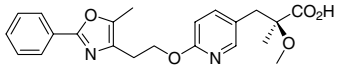
(*S*)-13

A novel series of potent dual PPARα/γ agonists was identified. SAR studies led to the identification of a multitude of compounds with varied isoform selectivity.

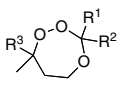
A novel series of potent dual PPARα/γ agonists was identified. SAR studies led to the identification of a multitude of compounds with varied isoform selectivity.



(*S*)-19

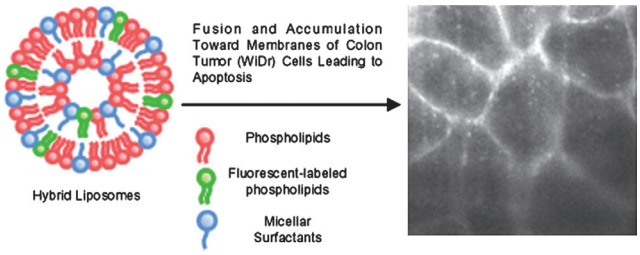


(*S*)-14

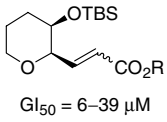


R^1, R^2 = $(CH_2)_4$ or $(CH_2)_5$ or Adamantylidine
R^3 = CH_2-SAr, Ar = *p*-Cl-Ph
or R^3= CH=CHCONEt_2
or R^3= CH=CHCO_2Me

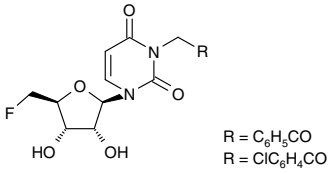
Thiol-olefin co-oxygenation (TOCO) of substituted allylic alcohols generates β-hydroxy peroxides that can be condensed in situ with various ketones, to afford a series of functionalised 1,2,4-trioxepanes in good yields. Manipulation of the phenylsulfenyl group in **8a**–**8c** allows for convenient modification to the spiro-trioxepane substituents.



A good correlation between 50% inhibitory concentration of hybrid liposomes (HL) on the growth of human colon tumor cells and membrane fluidity of HL was obtained.



The synthesis and in vitro antitumor activity of a series of enantiomerically pure (2*R*,3*R*)-disubstituted tetrahydropyrans against human solid tumor cells are reported.



A rapid fluorination at the 5′-position of nucleosides derivatives is achieved within 45 min providing yields of 75–92% by application of microwave.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

View of the crystal structure of the DB819-d(CGCGAATTCGCG)$_2$ complex, looking down the minor groove of the DNA (see Campbell, N.H.; Evans, D.A.; Lee, M.P.H.; Parkinson, G.N.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 15). The DB819 molecule is shown in space-filling mode. Visualisation produced with the VMD program. [Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* **1996**, *14*, 33.]

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