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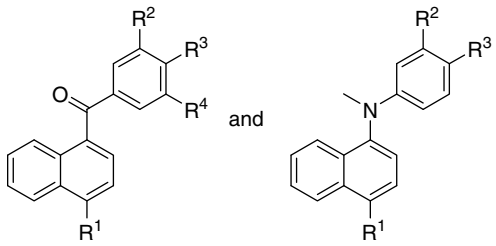
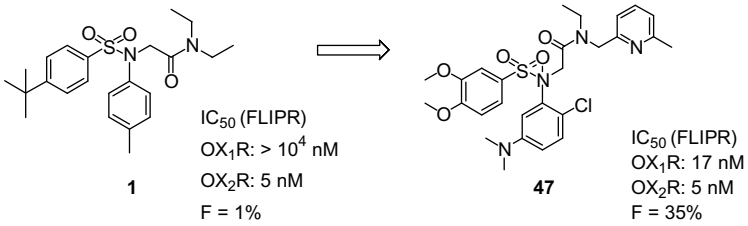
Contents

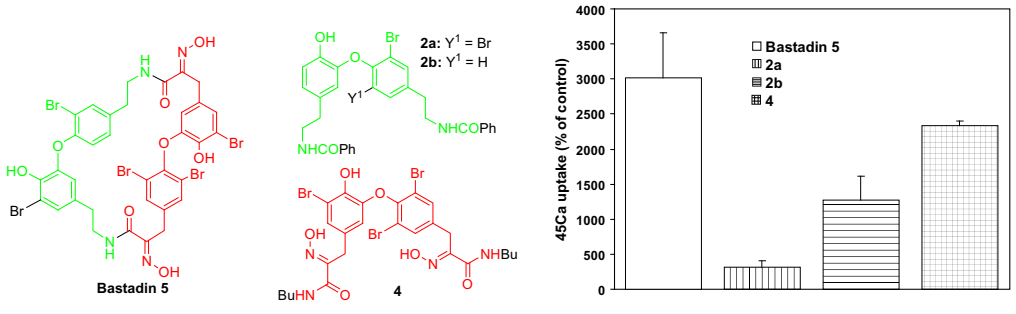
ARTICLES

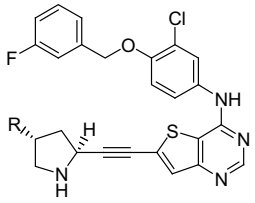


The discovery and SAR studies of (naphthalen-4-yl)(phenyl)methanones and *N*-methyl-*N*-phenylnaphthalen-1-amines as novel and potent apoptosis inducers is reported.

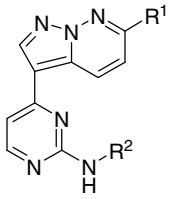


The structure–activity relationship and the synthesis of novel *N*-glycine-sulfonamides as OX_1R/OX_2R dual orexin antagonists are described. Compound **47** exhibited good oral bioavailability and has demonstrated in vivo activity in rats following oral administration.

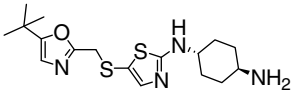




A novel class of substituted pyrrolidinyl-acetylenic thieno[3,2-*d*]pyrimidines has been identified that are potent and selective inhibitors of both EGFR/ErbB-2 receptor tyrosine kinases. The inhibitors are found to display a range of enzyme and cellular potency and also to display a varying level of covalent modification of the kinase targets. Selected molecules, including compound **15h**, were found to be potent in enzymatic and cellular assays while also demonstrating exposure in the mouse from an oral dose.



A novel series of pyrazolo[1,5-b]pyridazines have been synthesized and identified as cyclin dependant kinase inhibitors potentially useful for the treatment of solid tumors. Modification of the hinge-binding amine or the C(2)- and C(6)-substitutions on the pyrazolo[1,5-b]pyridazine core provided potent inhibitors of CDK4 and demonstrated enzyme selectivity against VEGFR-2 and GSK3β.



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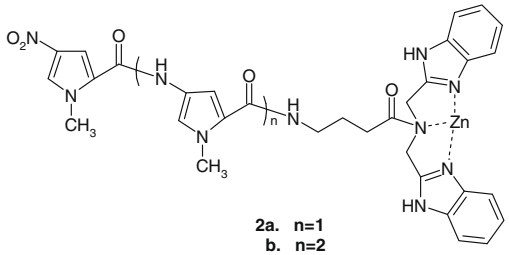
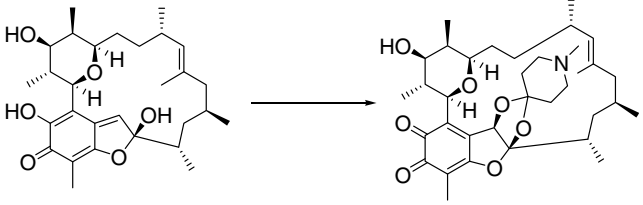
The identification of a selective CDK2, 7, 9 inhibitor **4** with improved permeability is described. The in vitro and PK properties of **4** are discussed.



2a. n=1
b. n=2
c. n=3

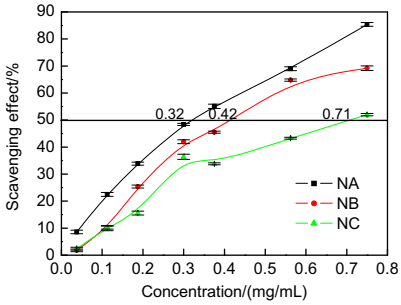
The synthesis and biological evaluation of Zn (II)–IDB complexes **2** as potent artificial nuclease are reported.

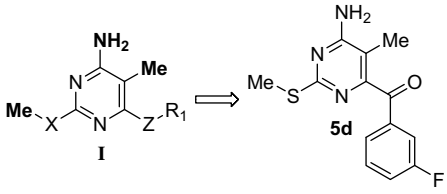
Discovery of a stable and soluble Bcl-xl inhibitor derived from kendomycin has been disclosed.

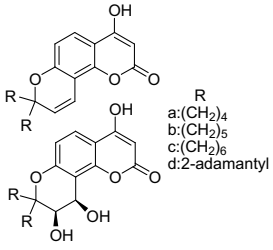


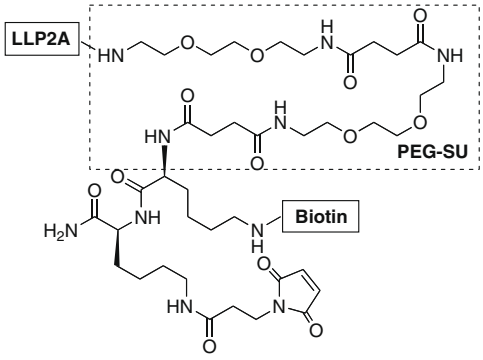
Kendomycin
Bc-xl IC_{50} =12.3μM
poor solubility
unstable

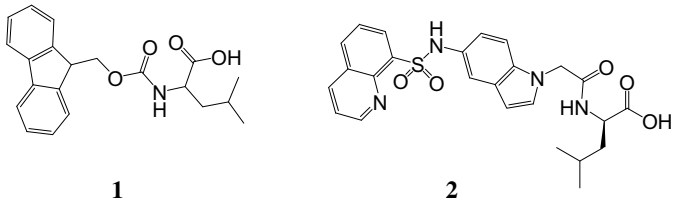
Bc-xl IC_{50} = 5μM
soluble and stable





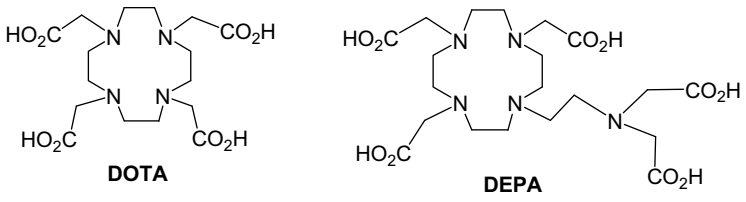




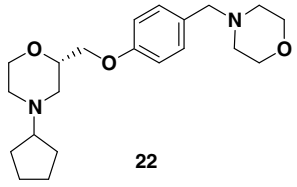


1 **2**

Two compounds were identified to produce partial agonist activity with potency in the moderate micromolar range as a result of ligand-based virtual screening.



DOTA **DEPA**



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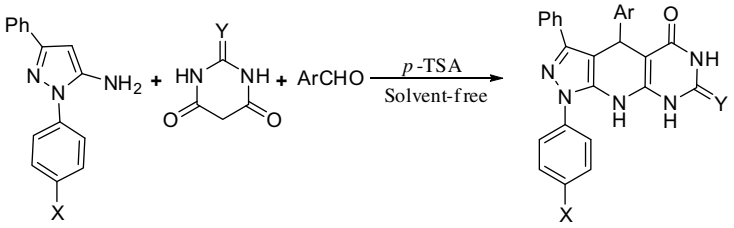
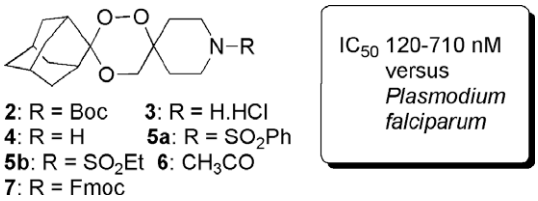
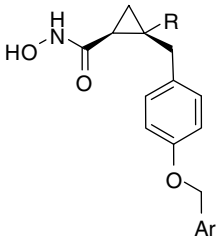
H_3 K_i =1.9 nM, pA_2=9.42

2-Aryloxymethylmorpholines are potent histamine H_3 antagonists.

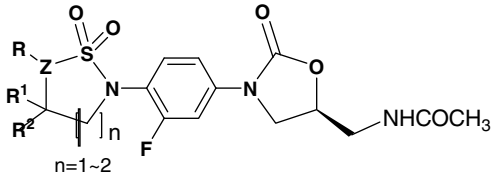




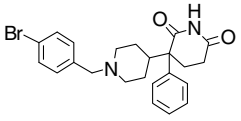
Dispiro *N*-Boc-protected 1,2,4-trioxanes were synthesised via $Mo(acac)_2$ catalaysed perhydrolysis of *N*-Boc spirooxirane followed by condensation of the resulting β-hydroperoxy alcohol with 2-adamantanone. *N*-Boc 1,2,4-trioxane was converted to the 1,2,4-trioxane hydrochloride salt which was subsequently used to prepare piperidine dispiro-1,2,4-trioxane analogues which were assayed versus *Plasmodium falciparum* in vitro.



We herein disclose a novel series of cyclopropyl hydroxamates that are potent and selective TACE inhibitors with K_i values in the picomolar range.



The synthesis of a new series of oxazolidinones having cyclic sulfonamide moieties is described. Their in vitro antibacterial activities against both Gram-positive and Gram-negative bacteria were tested and the effect of substituents on the oxazolidinone ring was investigated. A particular compound **15g** having [1,2,5]thiadiazolidin-1,1-dioxide moiety showed the most potent antibacterial activity.



A novel class of CXCR3 antagonist is explored for its key contributing moieties toward its potency and selectivity regarding unwanted anti-cholinergic activity.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Overlay of high resolution co-crystal structures of *R*-**22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5677.]

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