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Medicinal
Chemistry
Letters

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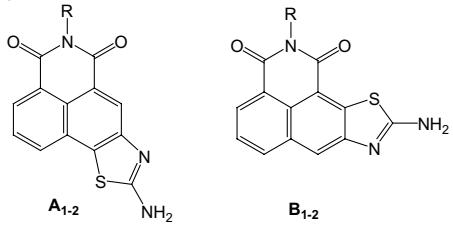
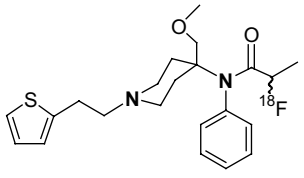
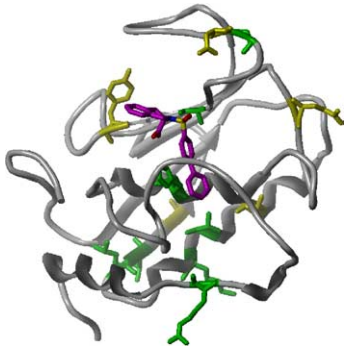
Contents

COMMUNICATIONS

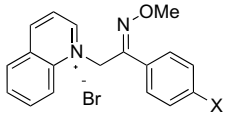


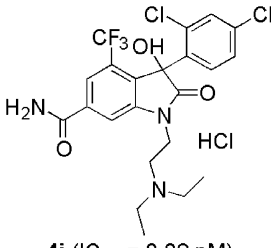
A_1, B_1: $R=CH_2CH_2N(CH_3)_2$
A_2, B_2: $R=CH_2CH_2CH_2N(CH_3)_2$





An NMR strategy for insights on residues influencing biological affinity is presented.

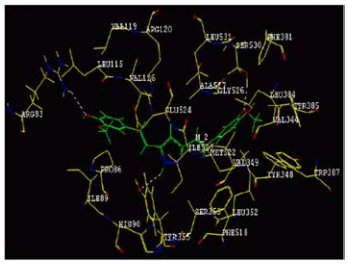


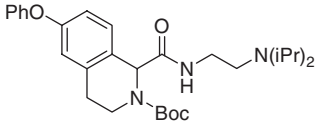


4i (IC_{50} = 0.02 nM)

The synthesis and the structure–activity relationships of a series of oxindole-based growth hormone secretagogues are reported. Compound **4i** was found to have potent in vitro and in vivo activity.

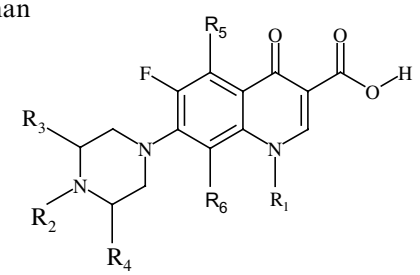
Curcuminoids were isolated from *Curcuma longa* and their pyrazole and isoxazole analogues were synthesized and evaluated for antioxidant, COX-1/COX-2 inhibitory and anti-inflammatory activities. Molecular docking study revealed the binding orientations of curcumin analogues in the active sites of COX-1 and COX-2.



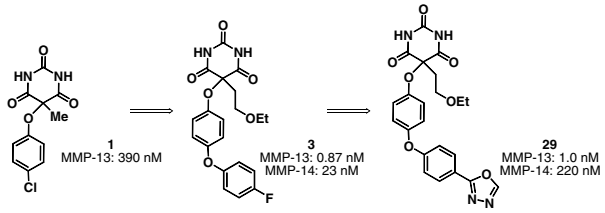


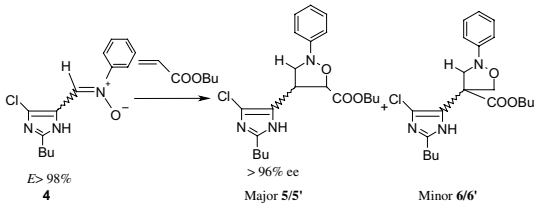
12a-E2 (EC_{50} = 0.46 nM)

Several novel series of tetrahydroisoquinoline 1-carboxamides (i.e., **12a**–**E2**) were prepared and shown to be potent growth hormone (GH) secretagogues.

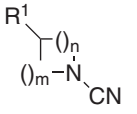


Synthesis and in vivo anti-tubercular activity of 6,8-difluoro-1-alkyl-5-amino-1,4-dihydro-4-oxo-7-{4-substituted piperazin-1-yl}-quinoline-3-carboxylic acids is reported.

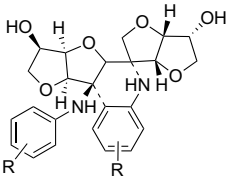




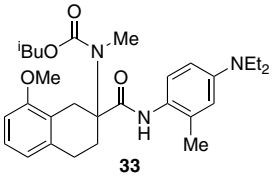
The *trans* rich isomer, 2-(phenyl)-3-(2-butyl-4-chloro-1*H*-imidazolyl)-5-butylate isoxazolidine (>96% ee) was synthesized by the condensation of *E* isomer rich nitrone (>98% ee) with butyl acrylate in an inert solvent. Thus obtained isoxazolidine was screened for its antifungal activity against *Aspergillus niger*, *Cephalosporium acremonium*, *Fusarium moniliforme* by using nystatin as positive control. It was also tested for its antibacterial activity against *Bacillus subtilis*, *Escherchia coli*, and *Staphylococcus aureus* by using streptomycin as a positive control. Enhanced antifungal activity was observed in isoxazolidine of >96% ee compared to the isoxazolidine of >69% ee, which was reported previously, and enhancement was not observed in antibacterial activity.



Starting from a PDE IV inhibitor hit derived from high throughput screening of the compound collection, a key pyrrolidine cyanamide pharmacophore was identified. Modifications of the pyrrolidine ring produced enhancements in cathepsin K inhibition. An X-ray co-crystal structure of a cyanamide with cathepsin K confirmed the mode of inhibition.

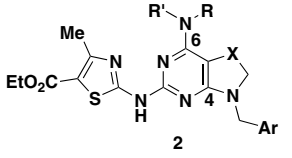


R= *p*-CH_3, *p*-OCH_3,
H, *p*-OH, *m*-CH_3



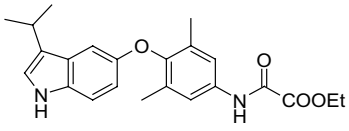
33

GHS-R binding IC_{50} 0.010 μM
FLIPR IC_{50} 0.033 μM
F 21%

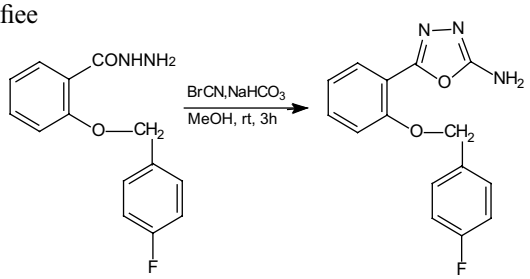


2

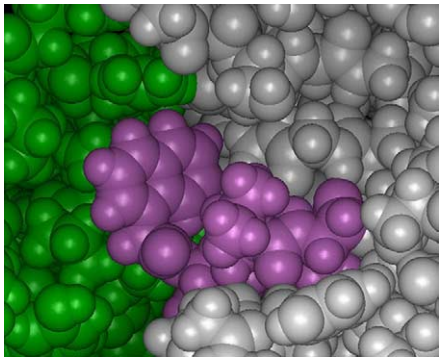
where X=CH_2, CH_2CH_2, OCH_2



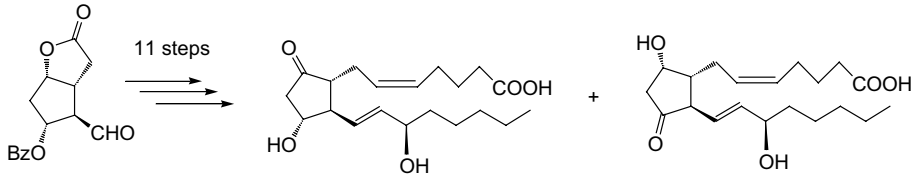
8, EC_{50}=4nM



1,3,4-Oxadiazole derivatives were synthesized as anticonvulsant agents. The anticonvulsant activity of the synthesized compounds was determined through PTZ and MES tests.

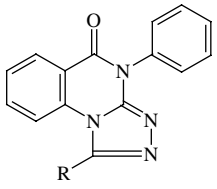


We describe herein the structure-based design of derivatives of tyropeptin A as the inhibitors of mammalian 20S proteasome.

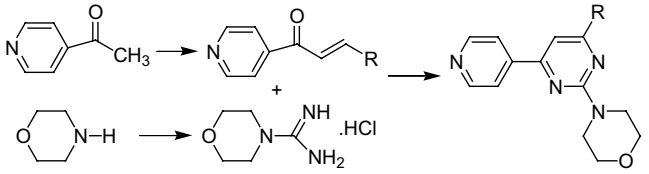


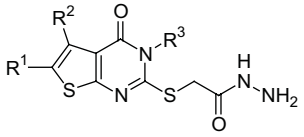
15R-PGE$_2$ **15R-PGD$_2$**

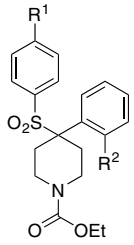
The first total synthesis of 15R-PGD$_2$ was accomplished. The approach used can be also an efficient method to produce 15R-PGE$_2$. The synthesis is part of a structure activity picture for the newly discovered PGD$_2$ receptor.

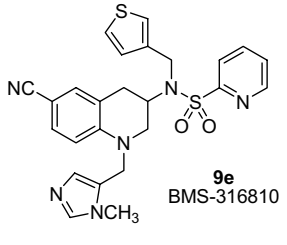


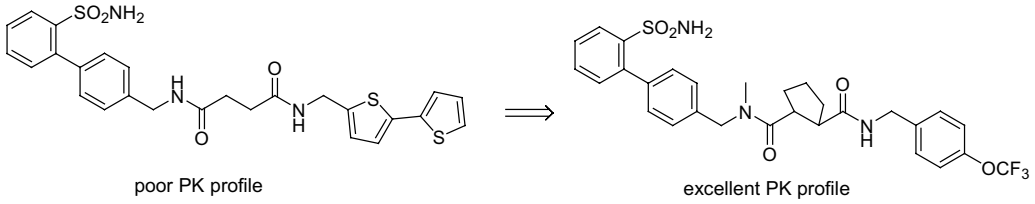
A series of novel 1-substituted-4-phenyl-1,2,4-triazolo[4,3-*a*]quinazolin-5(4*H*)-ones were prepared and evaluated for H$_1$-antihistaminic activity.

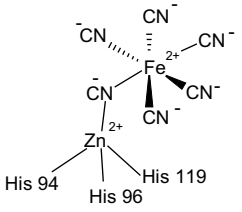


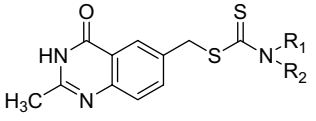




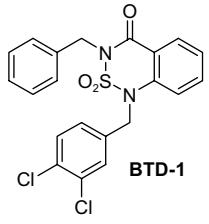




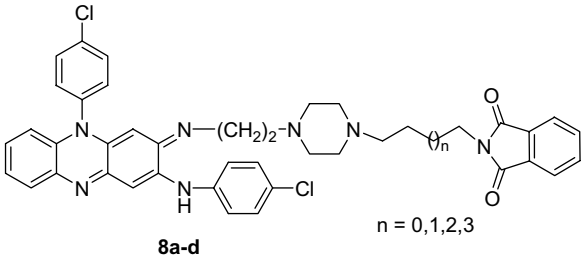




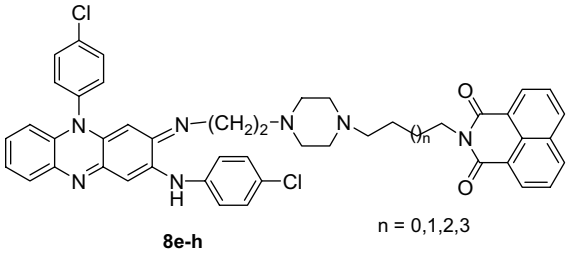
The synthesis and in vitro antitumor activity of a series of 4(3*H*)-quinazolinone derivatives is reported.



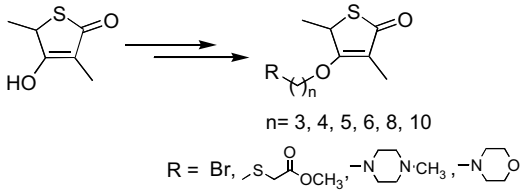
CODES neural networks and biopartitioning micellar chromatography (BMC) has been used to estimate the oral absorption of BTD derivatives and their efficacy has been verified.

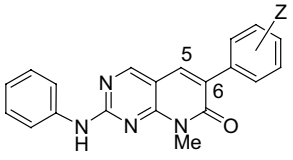


8a-d

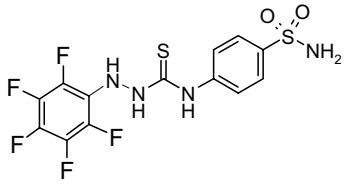


8e-h





2-Anilino-6-phenylpyrido[2,3-*d*]pyrimidin-7(8*H*)-ones are inhibitors of c-Src and Wee1 kinases. Selectivity for c-Src was not markedly changed by 6-phenyl ring substituents, but was lowered by 5-alkyl substituents.



OTHER CONTENTS

*Corresponding author

ⓘ+ Supplementary data available via ScienceDirect

COVER

A structure-based design approach was used to guide the evolution of an imidazopyridine scaffold yielding a new structural class of highly selective inhibitors of cyclin dependent kinases. The superposed structures of the original inhibitor (green, experimental data), the proposed inhibitor (yellow, computational model) and actual conformation of the bound inhibitor in CDK2 (blue, experimental data) is shown. [Hamdouchi, C.; Zhong, B.; Mendoza, J.; Collins, E.; Jaramillo, C.; De Diego, J. E.; Robertson, D.; Spencer, C. D.; Anderson, B. D.; Watkins, S. A.; Zhang, F.; Brooks, H. B. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1943.]

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