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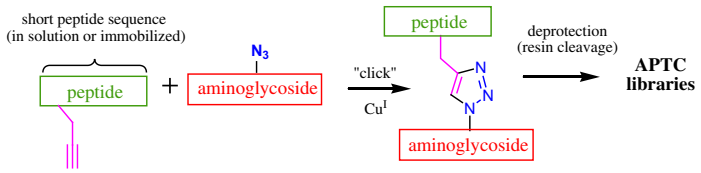
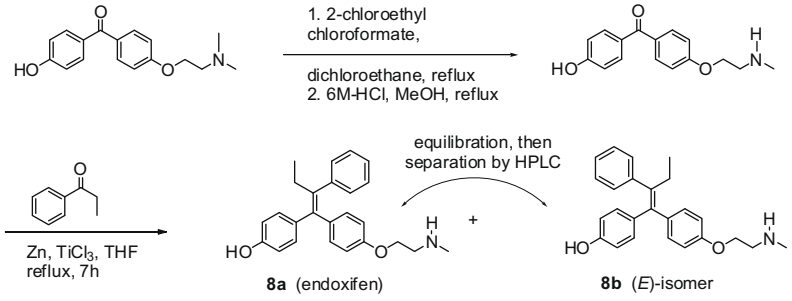
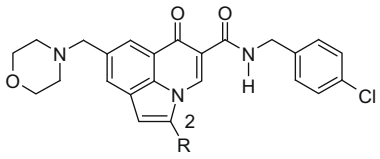
Contents

ARTICLES

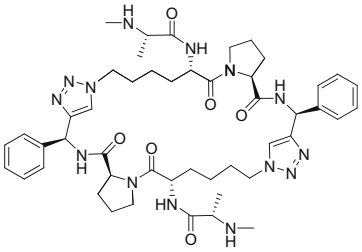


Synthesis of aminoglycoside–peptide triazole conjugates (APTCs) and their antibacterial evaluation is reported.

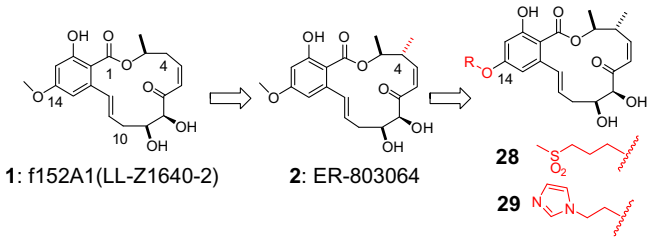


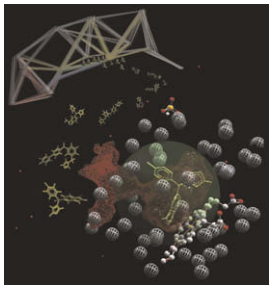


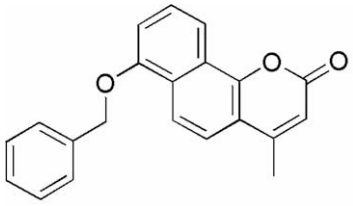
The synthesis of pyrroloquinoline analogs at C-2 with broad-spectrum anti-herpetic activity and improved solubility are reported.



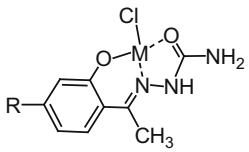
SM-162 (IC_{50} = 0.43 nM to XIAP;
K_i = 11 nM to cIAP-1; K_i = 24 nM to cIAP-2)





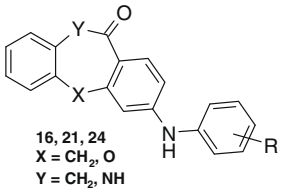


Novel benzocoumarin derivatives were synthesized and their hypolipidemic activity was evaluated resulting in identification of a potential lead.

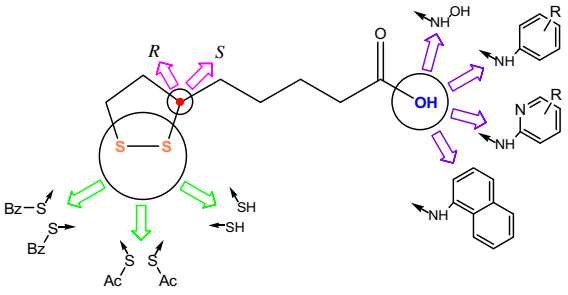


M = Cu (II), Zn
R = H, OH, MeO

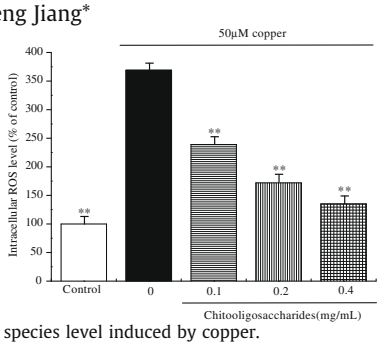
A series of copper(II) and zinc complexes of 2-hydroxyacetophenone semicarbazones have been prepared and evaluated as superoxide dismutase (SOD) mimetics.



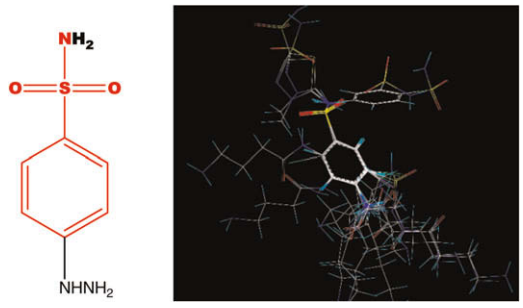
p38 MAP Kinase is an attractive and promising drug target for novel anti-inflammatory therapeutics. In this paper we present a novel, efficient synthesis route to obtain chloro-substituted 5,11-dihydro-dibenzo[*a*,*d*]cyclohepten-10-ones. Investigations of the inhibitory activities and structure–activity relationship of tricyclic inhibitors for p38 MAP kinase were accomplished.

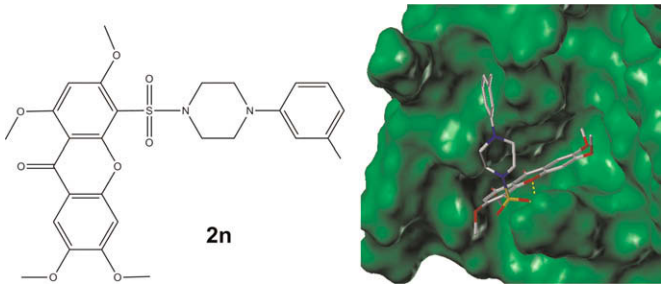


α-Lipoic acid derivatives were synthesized and their anticancer activities were evaluated.

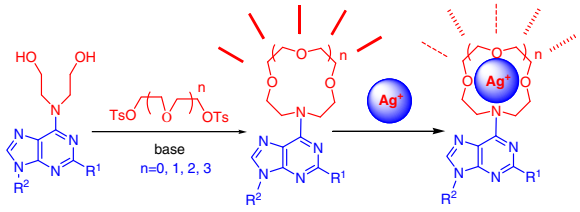


Chitooligosaccahrides attenuating intracellular reactive oxygen species level induced by copper.

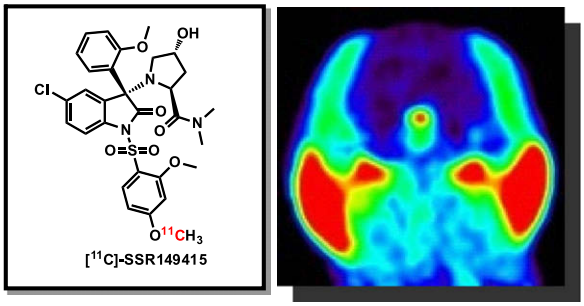


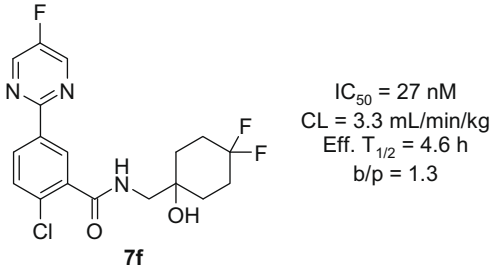


A series of xanthone sulfonamides were identified by HTS as inhibitors of the ACAT. Compound **2n** shows 64.8% inhibition to ACAT at 10 μg/mL concentration.



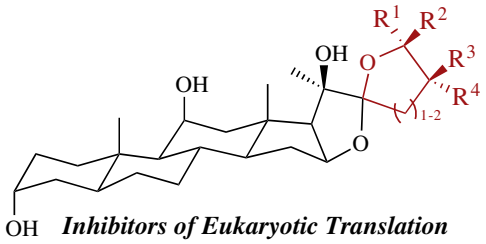
The synthesis and fluorescence properties of novel purine analogues linked azacrown ether at C6 position were investigated. These new purine analogues could be prepared from a series of 6-chloropurines and showed selective and efficient signaling behaviors toward micromolar concentration of Ag^+ ion over other common metal ions in an aqueous environment.



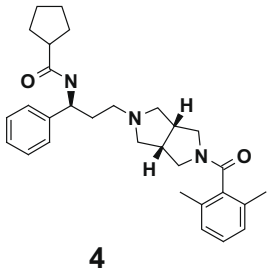


7f

The discovery of a potent P2X$_7$ receptor antagonist, **7f**, with excellent CNS exposure and PK profile is reported.



Inhibitors of Eukaryotic Translation



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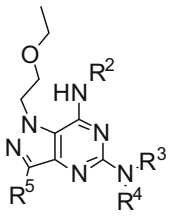
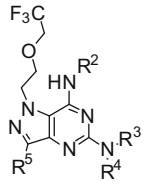
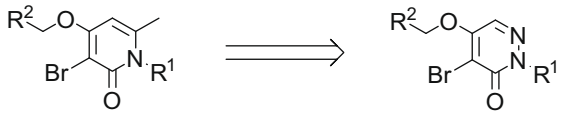


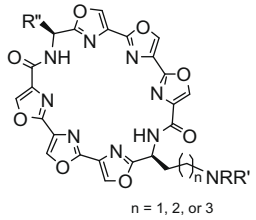
This work explores the potency, selectivity and efficacy of 1-(2-ethoxyethyl)-1*H*-pyrazolo[4,5-*d*]pyrimidines as PDE5 inhibitors resulting in the advancement of a clinical candidate.



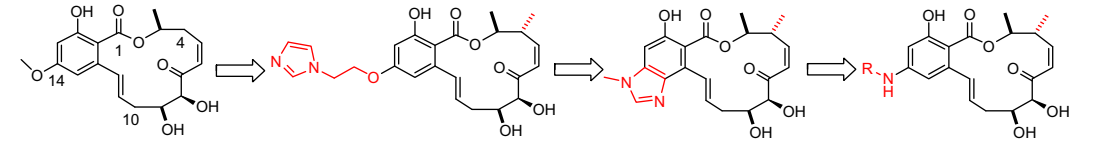
This work explores the advancement of more selective and potent PDE5 inhibitors resulting from the substitution of 2-(2,2,2-trifluoroethoxy)ethyl at the 1-position of 1*H*-pyrazolo[4,3-*d*]pyrimidines.

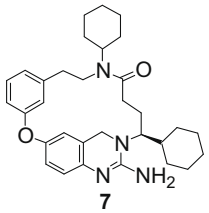


The synthesis, structure–activity relationship and modeling of a series of 5-substituted-*N*-aryl pyridazinone based p38α inhibitors are described. In comparing the series to the similar *N*-aryl pyridinone series, it was found that the pyridazinones maintained a weaker interaction to the p38 enzyme, and therefore showed generally weaker binding than the pyridinones.

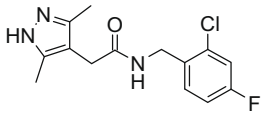


Several monoaminoalkyl derivatives with R″ being isopropyl and various *bis*-aminoalkyl substituted hexaoxazoles derivatives were evaluated for cytotoxicity and stabilization of G-quadruplex RNA and DNA. One of the more cytotoxic analogs (where $n = 1$, R″ is isopropyl and both R and R′ are methyl substituents) inhibits human tumor growth in the athymic nude mouse xenograft model.





Structural biology allowed the identification of **7** as a potent BACE inhibitor (IC_{50} = 5 nM).



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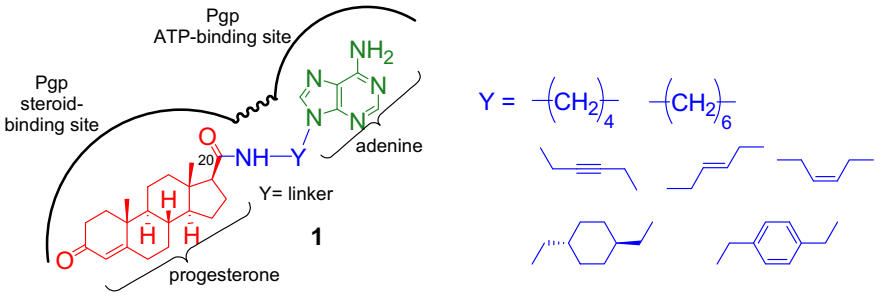
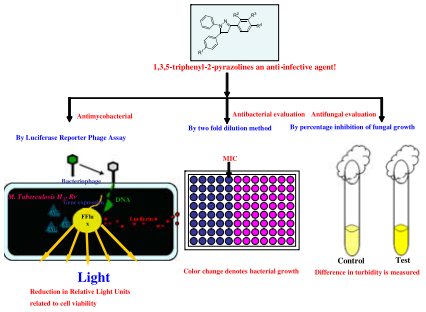
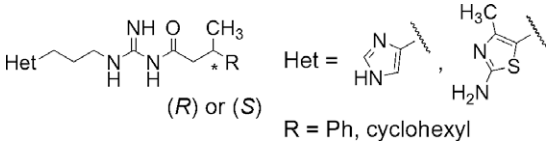
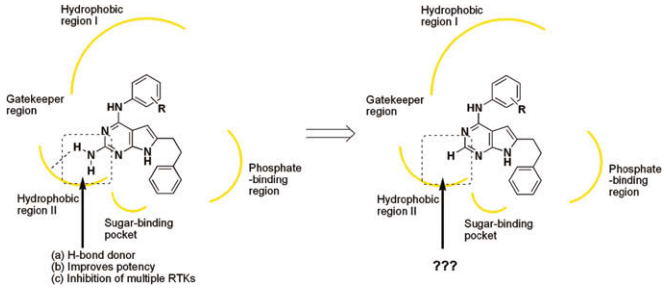
Human P2X$_7$ pIC$_{50}$ 7.7



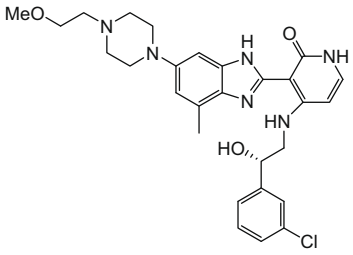




The synthesis and pharmacological characterisation of the enantiomers of the title compounds on recombinant histamine receptors (gpH$_2$R and hH$_2$R, hH$_1$R, hH$_3$R, hH$_4$R) and on the isolated guinea pig atrium is described.



A series of 3-[6-(4-substitued-piperazin-1-yl)-4-methyl-1*H*-benzimidazol-2-yl]-1*H*-pyridine-2-one were synthesized to modulate CYP3A4 inhibition and improve aqueous solubility of our prototypical compound BMS-536924 (**1**), while maintaining potent IGF-1R inhibitory activity. Structure–activity and structure–solubility studies led to the identification of BMS-577098 (**27**), which demonstrates oral in vivo efficacy in animal models. The improvement was achieved by replacing morpholine with more polar bio-isoster piperazine and modulating the basicity of distal nitrogen with appropriate substitutions.



BMS-577098

OTHER CONTENT

*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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