ELSEVIER

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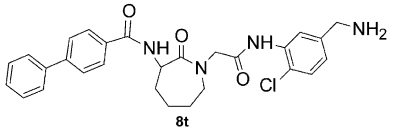
Bioorganic & Medicinal Chemistry Letters

# Contents

## COMMUNICATIONS

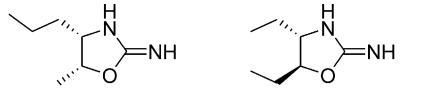





8t

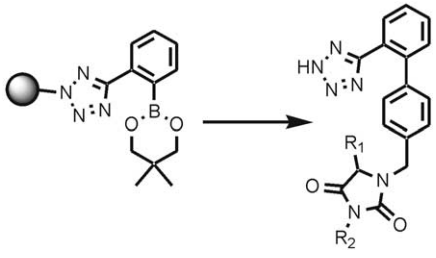
The synthesis, employing solution phase parallel methods, and SAR of a series of novel 2-azepanones are descibed leading to identification of **8t** as a potent inhibitor of human tryptase with high selectivity versus related serine proteases including trypsin.





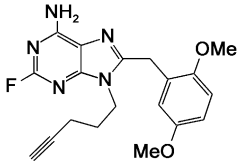

(+/-)-**5d** $IC_{50}$ = 41 nM (+/-)-**6c** $IC_{50}$ = 56 nM





A convenient and efficient palladium-catalysed retro-ene-assisted method has been developed to prepare a series of 5-substituted-6-phenyl-3(2*H*)-pyridazinones as potential antiplatelet drugs. The most active compounds were those that contain a 3-phenyl-3-oxo-propenyl fragment or a phenylthio group at position 5 of the heterocyclic ring.

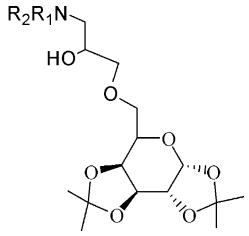





**11**

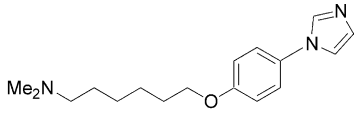
Several new crystal structure complexes of Hsp90 with known and new ligands explain the observed SAR for the series.





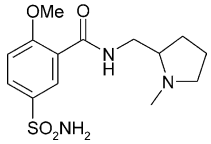

A series of glactopyranosyl amino alcohols have been synthesised and evaluated against *Mycobacterium tuberculosis* and one of them was found to be superior to ethambutol.



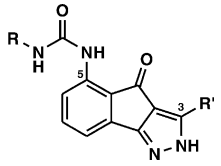



**3g** : $IC_{50}$ 8.8nM

This paper describes the design and synthesis of 1-alkoxyphenyl)imidazole derivatives as CYP-selective 20-HETE synthase inhibitors.





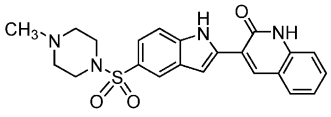




The synthesis and evaluation of indeno[1,2-*c*]pyrazol-4-one with heterocycles at C3 are described.

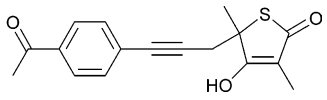


Clotrimazole (CLT) **1**, a synthetic anti-fungal imidazole derivative, inhibits tumor cell proliferation and angiogenesis. In the current study, flow cytometric analysis demonstrated that the decrease in tumor cell growth by CLT **1** was associated with inhibition of cell cycle progression at the $G_1$-S phase transition, resulting in $G_0$-$G_1$ arrest. A series of CLT **1** analogues has been generated in order to develop CLT **1** derivatives that are devoid of the imidazole moiety which is responsible for the hepatoxicity associated with CLT **1** while retaining CLT **1** efficacy. The majority of these analogues demonstrate in vitro antiproliferative activity ranging from submicromolar to micromolar concentrations.

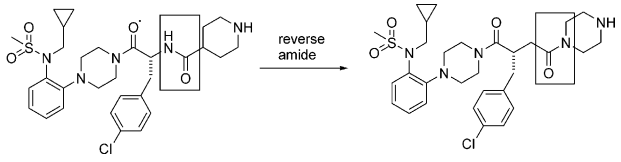





**14**, KDR $IC_{50}$ = 10 nM
Dog PK: Cl = 0.5 mL/min/kg,
$t_{1/2}$ = 6.4 h, %F = 63%
hERG IP = 3440 nM

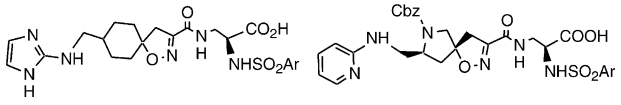




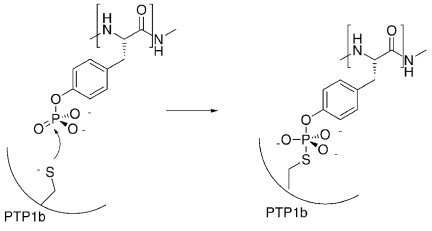


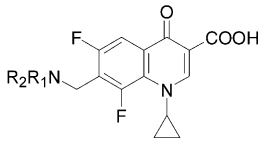

A novel series of piperazines appended to a succinamide backbone were synthesized and found to have a high affinity for the melanocortin-4 receptor ($IC_{50}$s ranging from $<0.1$ to 200 nM). Both agonists and antagonists of MC4R were prepared by modifying the groups attached to the right-hand side of the succinamide. This series also exhibits a high level of selectivity (up to 7000-fold) over mouse MC1R and human MC3R.





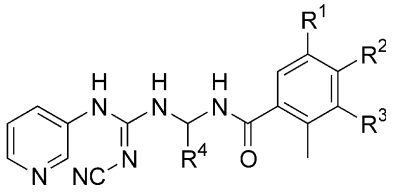






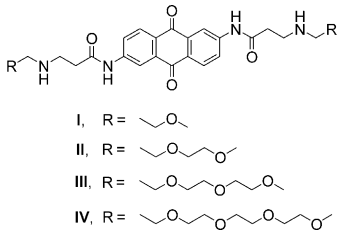

A series of 7-(substituted)aminomethyl quinolones was synthesized and evaluated for antibacterial activity. Some derivatives exhibited high potency comparable to Lomefloxacin and Vancomycin.





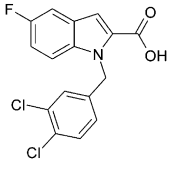

Novel cyanoguanidines which hyperpolarize human bladder $K_{ATP}$ channels are reported.

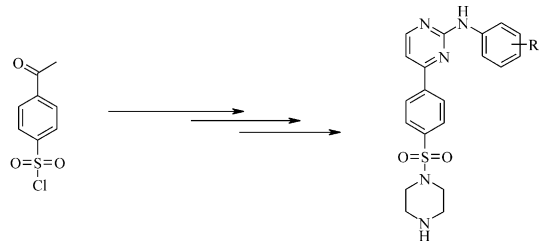




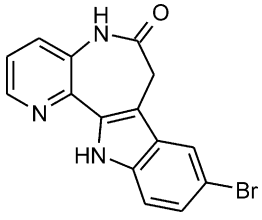

The binding of a series of homologous 2,6-disubstituted anthraquinones to DNA is a function of the length of the side chain.



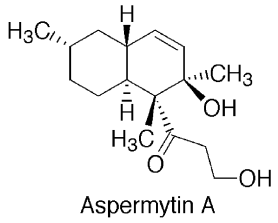








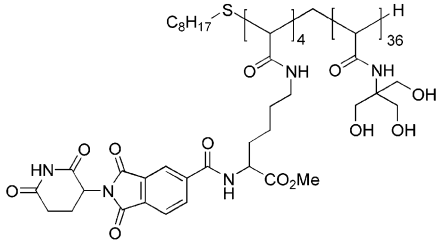




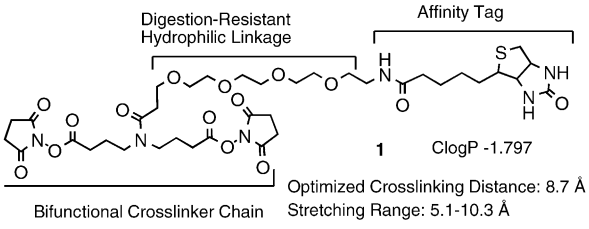
Aspermytin A

A new polyketide, aspermytin A, was isolated from a cultured marine fungus, *Aspergillus* sp., which was separated from the mussel, *Mytilus edulis*. It induced neurite outgrowth in rat pheochromocytoma (PC-12) cells as concentration of 50 μM.





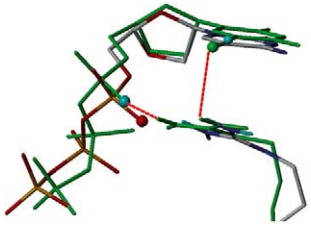
Synthesis and biological assessments of THAM derived telomers bearing thalidomide moieties as antiangiogenic drug.





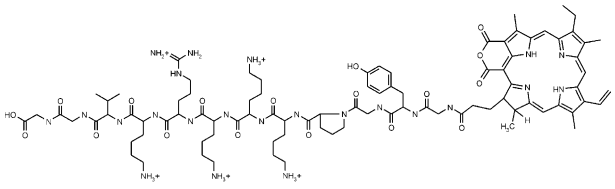

Edunol (**3**), a pterocarpan isolated from *Harpalyce brasiliana*, a plant used in the northeast of Brazil against snakebites, was obained by synthesis and showed antimyotoxic, antiproteolytic and PLA2 inhibitor properties. These proprieties could be improved through the synthesis of a bioisoster (**5**), where the prenyl group was replaced by the benzyl group.

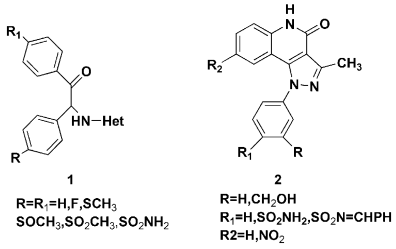




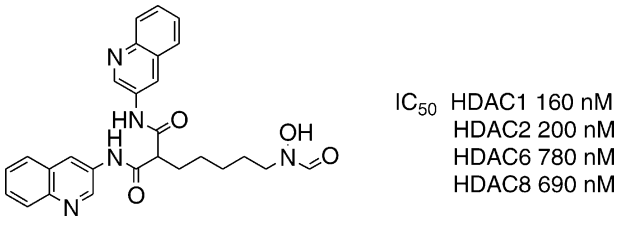
The molecular dynamics simulation of various fluorine-substituted nucleoside triphosphate analogues complexed with HIV-1 RT is presented.





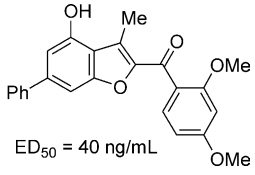




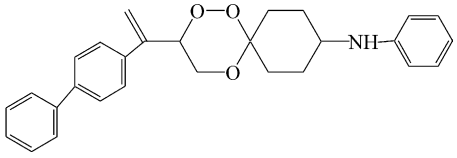

Hybrid polar compounds with a *N*-formyl hydroxylamino head group were synthesized and tested for HDAC inhibitory activities.

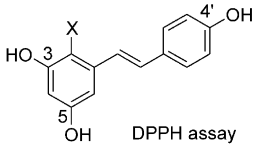





A lead optimization program was carried out on a screening hit to discover novel type of anti-tumor agents.



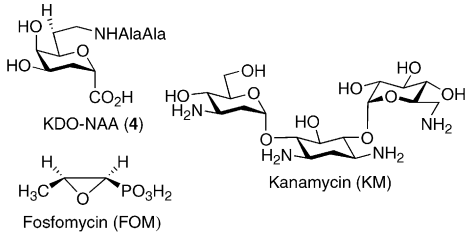





| DPPH assay | $IC_{50}$ (μmol) |
|---|---|
| X = H, resveratrol | 123.3 |
| X = Br | 35.9 |

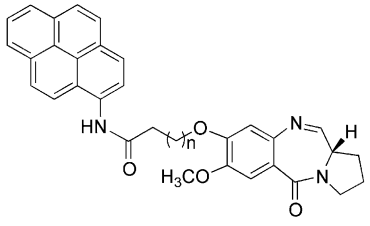
Nine new resveratrol derivatives, were designed and synthesized. Among them, 2-bromoresveratrol **19** has a similar free radical scavenging activity to (+)-catechin.



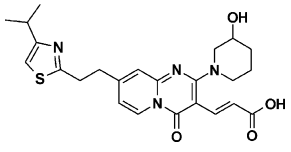


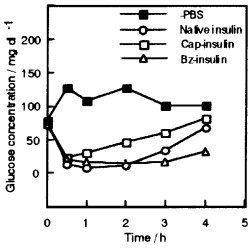

Synergistic effect of CMP:KDO synthase inhibitors (**4**) with both KM and FOM on inhibition of release of vero toxin by *Escherichia coli* O157 was observed.





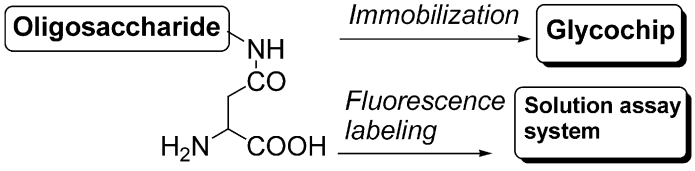




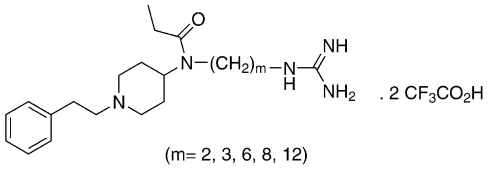

Hypoglycemia effects of acylated insulin with benzoyl groups (Bz-insulin) almost similar to that of native insulin was obtained in the animal experiments using normal rats in vivo.





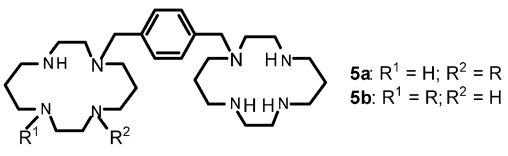

A glycochip containing the whole structure of an oligosaccharide was easily prepared by the immobilization of the glycosylasparagines. Furthermore, fluorescence-labeled glycosylasparagines were used to analyze carbohydrate–lectin interaction in a solution assay system by fluorescence polarization (FP) and fluorescence correlation spectroscopy (FCS).



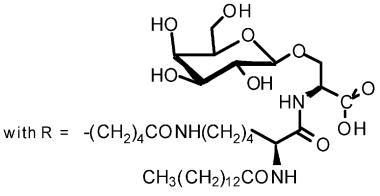


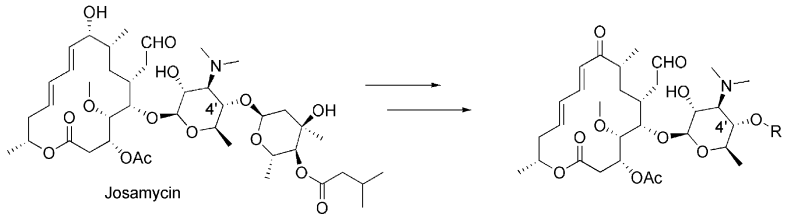

A new series of fentanyl derivatives bearing aliphatic alkaneguanidinium moieties were prepared. Their affinities for the μ opioid receptors and for the $I_2$-imidazoline binding sites (IBS) were determined on human post-mortem prefrontal cortex membranes. All of these hybrid compounds had significant and/or very high affinity for both receptors.



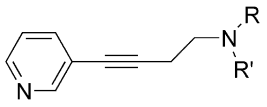



**5a**: $R^1$ = H; $R^2$ = R
**5b**: $R^1$ = R; $R^2$ = H



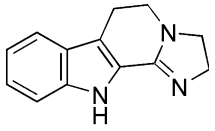





The binding of a series of pyridylbutynylamines at α4β2 nACh receptors was shown to be sensitive to, and dependent upon, the nature of ring and terminal amine substituents.

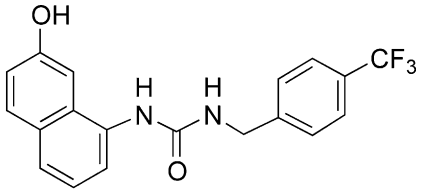





10

Imidazopyridoindole **10** ($I_2$ $K_i = 7.3$ nM) suggests how two structural classes of $I_2$ receptor ligands, 2-(2-benzofuranyl)-2-imidazolines and β-carbolines, might bind relative to one another.






**5f**

Structurally simple 7-hydroxynaphthalenyl ureas and amides were discovered to be potent ligands of human Vanilloid Receptor 1. 1-(7-Hydroxynaphthalen-1-yl)-3-(4-trifluoromethylbenzyl)urea **5f** exhibited nanomolar binding affinity and upon capsaicin challenge, behaved as a potent functional antagonist.

## 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 htB1 (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htB1 (center) allows for functional selection against thrombin (right). 



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