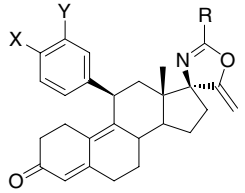
ELSEVIER

Bioorganic & Medicinal Chemistry Letters

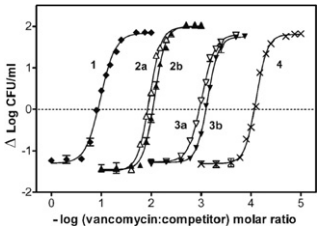
Bioorganic & Medicinal Chemistry Letters Vol. 17, No. 21, 2007

Contents

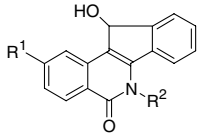
ARTICLES

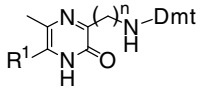


A series of novel 11β-aryl-4′,5′-dihydrospiro[estra-4,9-diene-17β,4′-oxazole] analogs have been synthesized and evaluated for their antiprogesterone and antiglucocorticoid activities.



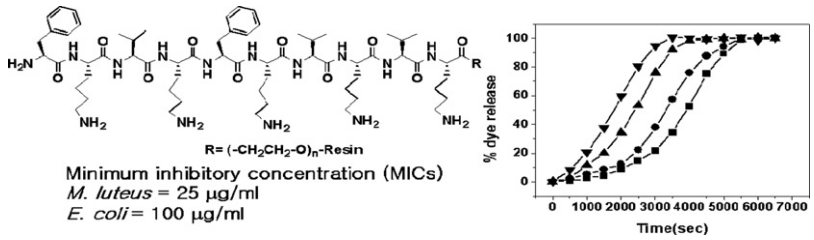
1: *N*-α-Ac-L-Lys-D-Ala-D-Ala tripeptide
2a: *N*-Boc-6-aminocaproyl-D-Ala-D-Ala
2b: *N*-Acetyl-6-aminocaproyl-D-Ala-D-Ala
3a: *N*-Boc-6-aminocaproyl-D-Ala-D-Ser
3b: *N*-Acetyl-6-aminocaproyl-D-Ala-D-Ser
4: D-Ala-D-Ala

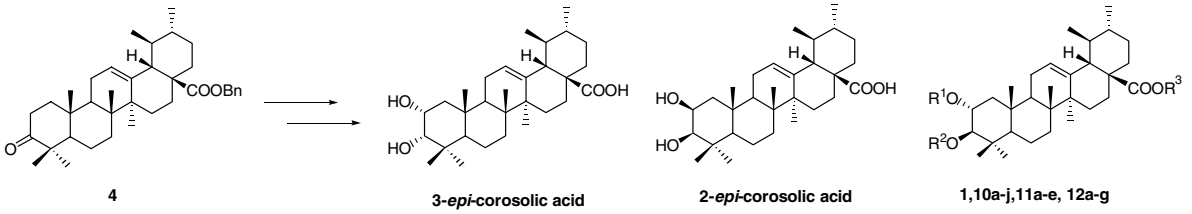




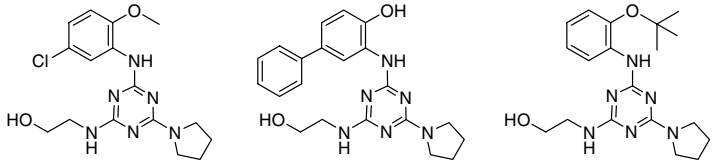
11 n = 4, R^1 = β-phenethyl

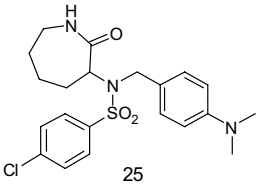
3-[4′-*H*-Dmt-NH-$(CH_2)_4$]-6-β-phenethyl-5-methyl-2(1*H*)-pyrazinone **11** bound to μ-opioid receptors, $K_i\mu = 0.13$ nM and $K_i\delta/K_i\mu = 447$, and exhibited μ-agonism (GPI $IC_{50} = 15.9$ nM) and δ-antagonism (MVD, $pA_2 = 6.35$).

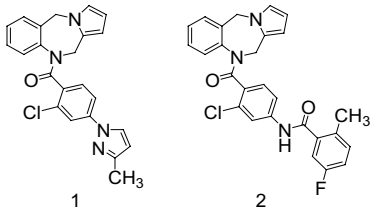




The synthesis and biological evaluation of corosolic acid derivatives as inhibitors of glycogen phosphorylases is described.

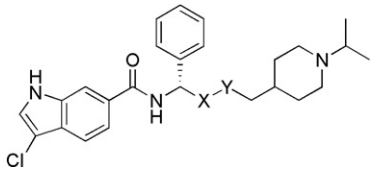


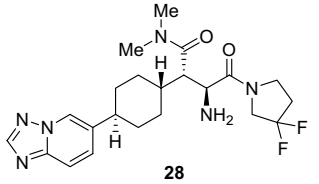




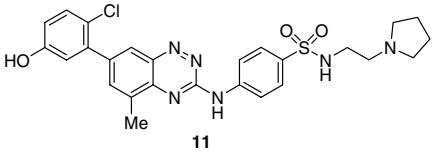
1 2

The synthesis and biological results for metabolites of the above vasopressin agonist **1** and antagonist **2** are presented.



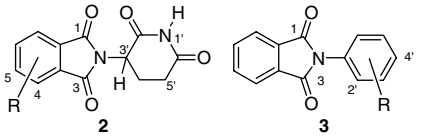


28
DPP-4 IC_{50} = 4.8 nM

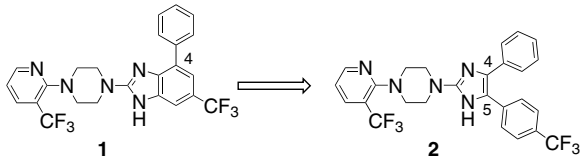


11

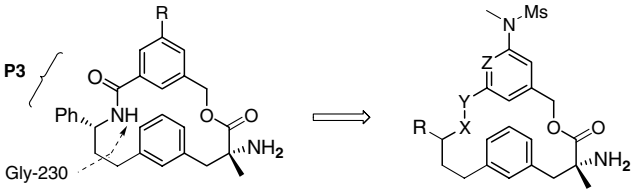
We describe the design, synthesis and structure–activity relationship studies in optimizing a series of benzotriazine compounds as potent inhibitors of both Abl and Abl-T315I enzymes.

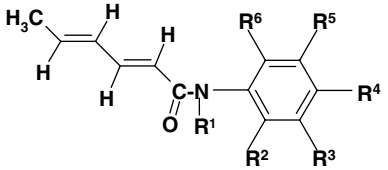


A series of novel thalidomide and *N*-phenylphthalimides were synthesised from their halide precursors using a Heck cross coupling reaction. This library of compounds was assessed for their ability to alter TNF production through measuring inhibition of TNF transcriptional activity.

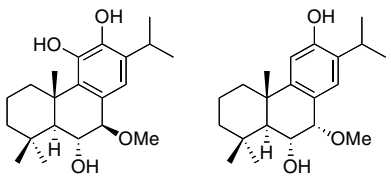


This letter describes replacements for the P3 amide moiety present in previously reported tertiary carbinamine macrolactones. Although P-gp efflux issues associated with these amide-macrolactones were solved and brain penetration was measured in one case, potency was compromised in the process.



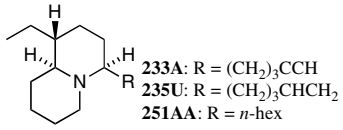


QSAR study of synthesized 2,4-hexadienoic acid derivatives as antimicrobial agents indicated the importance of the topological parameters especially the molecular connectivity indices ($^{0}\chi^{v}$, $^{2}\chi^{v}$, $^{2}\chi$) in contribution to antimicrobial activity.

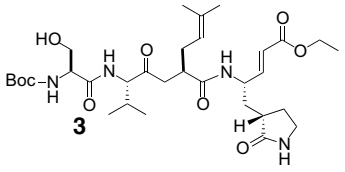


1 **2**

Two new abietane-type diterpenes, taxodistines A (**1**) and B (**2**), have been isolated by the guidance of inhibitory effect of tubulin polymerization from the fruits of *Taxodium distichum* and the structures were elucidated by using 2D NMR data. Taxodistine B (**2**) showed inhibition of tubulin polymerization.

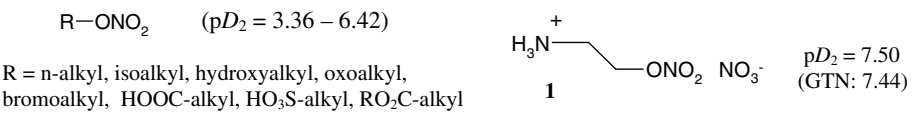


The synthesis and inhibitory effects on neuronal nicotinic acetylcholine receptors of the poison-frog alkaloids **233A**, **235U**, and **251AA** are described.



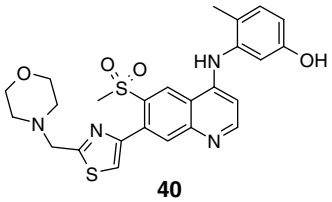
3

Structure-based design, synthesis, and biological evaluation of a series of peptidomimetic SARS-CoV 3CLpro inhibitors are described. Inhibitor **3**-bound SAR-3CLpro X-ray crystal structure provided molecular insight into the ligand-binding site interactions.



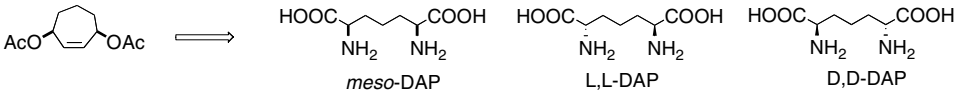
1

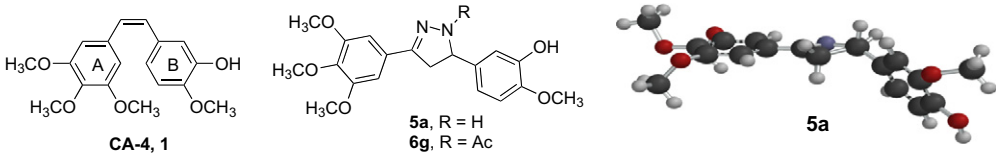
The vasoactive properties of 14 organic mononitrates were investigated in vitro using $PGF_{2\alpha}$-precontracted porcine pulmonary arteries. Activities showed to be highly sensitive to the structure and substituents. Compound **1** was found to be slightly superior to the high potency trinitrate GTN.

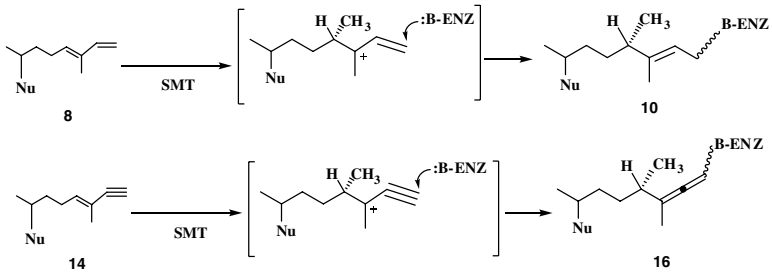


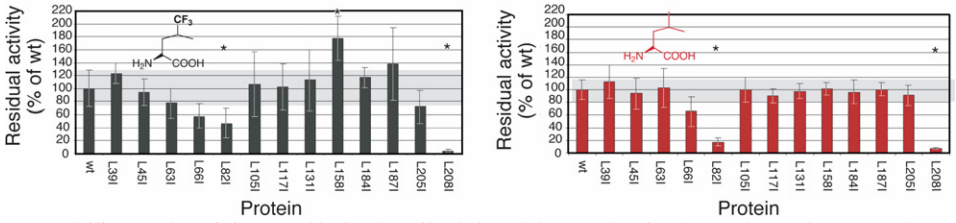
40

Substituted 4-(3-hydroxyanilino)-quinoline compounds, initially identified as small-molecule inhibitors of src family kinases, have been evaluated as potential inhibitors of RET kinase. Three compounds, **38**, **31**, and **40**, had K_i values of 3, 25, and 50 nM in an in vitro kinase assay; while a cell based kinase assay showed K_i values of 300, 100, and 45 nM, respectively. These compounds represent potential new leads for the treatment of medullary and papillary thyroid cancer.

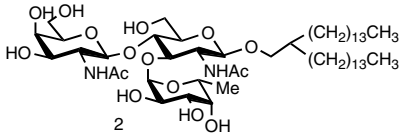




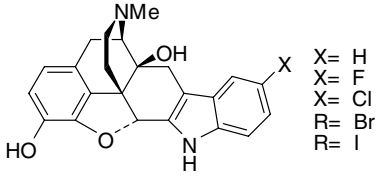


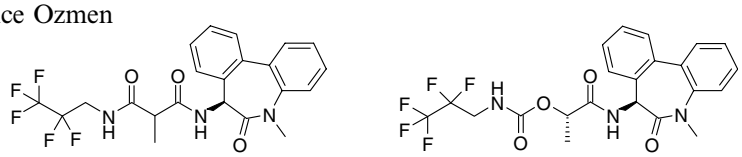


A lysate-based thermostability and activity profile is described for chloramphenicol acetyltransferase (CAT) expressed in trifluoroleucine, T (CAT T). CAT and 13 single-isoleucine CAT mutants were expressed in medium supplemented with T and assayed for thermostability.

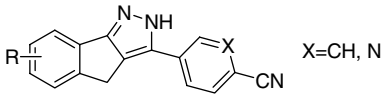


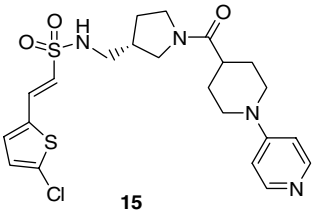
A novel glycosphingolipid analogue β-D-GalNAc*p*(1-4)[α-D-Fuc*p*(1-3)]-β-D-GlcNAc*p*(1-R) (**2**) and some non-natural type trisaccharide analogues were synthesized, and their ability to inhibit the nitric oxide release was also examined.





Malonamide analogues of LY411575 were found to be potent inhibitors of γ-secretase in vitro. The introduction of a pentafluoropropyl side chain improved the metabolic stability, and led to malonamide and carbamate analogues with in-vivo activity in models of Alzheimer's disease.

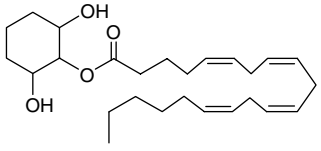




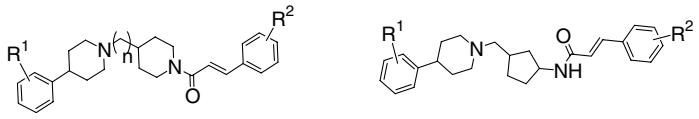
15

IC_{50} = 5.5 nM

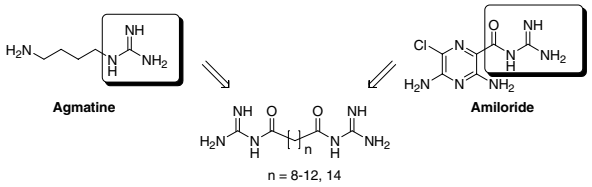
PT EC_{2x} = 1.7 μM

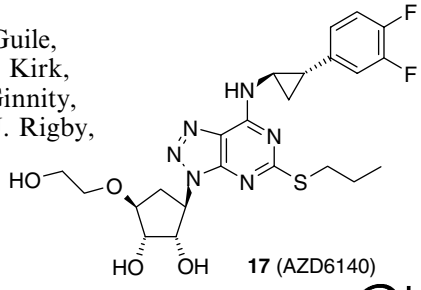


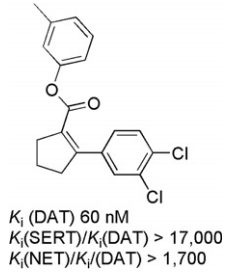
All isomeric 2-arachidonoyl esters of cyclohexane-1,2,3-triol were synthesized, tested as ligands for CB1 and CB2 receptors, and evaluated as substrates for both monoacylglycerol lipase (MGL) and fatty acid amide hydrolase (FAAH).

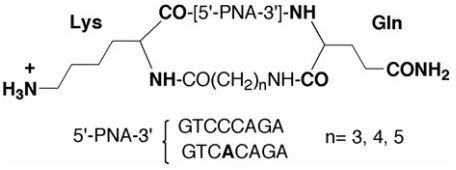


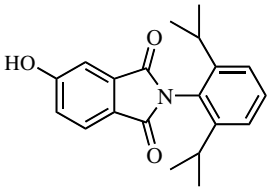
A series of phenyl piperidine derivatives have been synthesized and evaluated as CCR2 antagonists.











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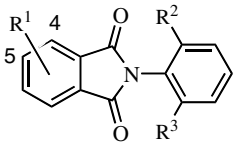

Compounds 1 - 20

R^1= 4 or 5 CH_3, Cl, CO_2H, CO_2CH_3, NH_2, NO_2, $NHCOCH_3$, OH, OSO_2NH_2

R^2, R^3 = H, Me, Et, Pr, iPr, iBu, F, Cl, Br

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

The binding of compound **11** at the ATP pocket of Abl-T315I mutant. The hydroxyl group of phenyl interacts with Glu286 from the αC-helix. The gatekeeper residue Ile-315 forms hydrophobic interactions with the aromatic ring of the benzotriazine. [Cao, J.; Fine, R.; Gritzen, C.; Hood, J.; Kang, X.; Klebansky, B.; Lohse, D.; Mak, C. C.; McPherson, A.; Noronha, G.; Palanki, M. S. S.; Pathak, V. P.; Renick, J.; Soll, R.; Zeng, B.; Zhu, H. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5812.]

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