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Bioorganic & Medicinal Chemistry Letters

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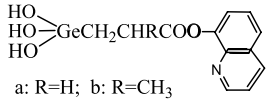
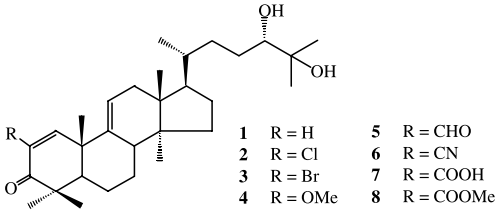
Contents

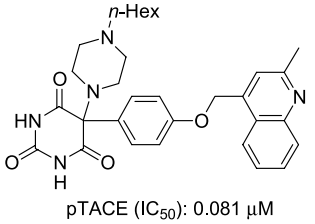
COMMUNICATIONS

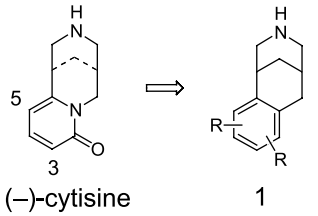


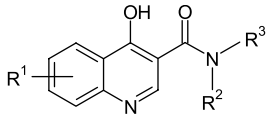
Two newly synthesized Ge132 derivatives can greatly enhance their DNA binding. Unexpected methyl substitution effect on DNA sequence selectivity and cytotoxicity was observed.



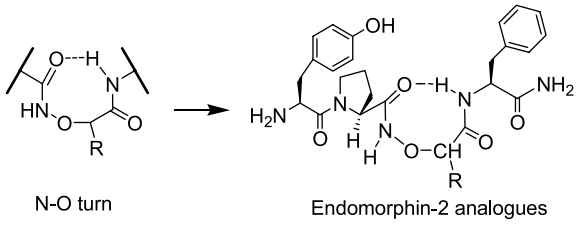
Lanostane-type triterpenoids with various functional groups (–Cl, –Br, –OMe, –CHO, –CN, –COOH, and –COOMe) at C-2 were synthesized from 3-oxolanost-9(11)-en-24*S*,25-diol isolated from *Pinus luchuensis* and their inhibitory effects on Topo II activity and cytotoxic activities against A549 cells were examined.

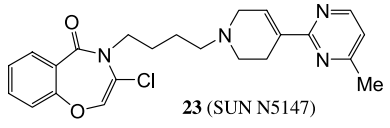




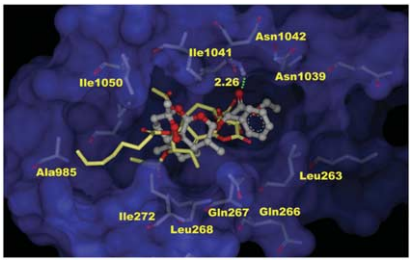


A series of novel quinoline-3-carboxamide derivatives were synthesized and evaluated for their immunomodulatory activity.

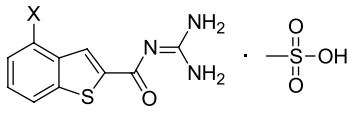




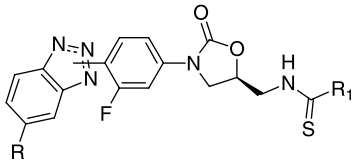
4-Methyl-2-(1,2,3,6-tetrahydropyridin-4-yl)pyrimidine derivative **23** (**SUN N5147**) exhibited sub-nanomolar affinity for 5-HT_{1A} receptor with 1000-fold selectivity over both dopamine D_2 and α_1-adrenergic receptors and remarkable neuroprotective activity in a transient middle cerebral artery occlusion model.



The structure of PfATP6 and docking of artemisinins to PfATP6 are reported.



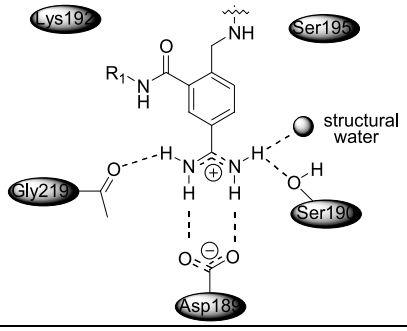
Synthesis and biological evaluation of 4-substituted (benzo[*b*]thiophene-2-carbonyl)guanidines as NHE-1 inhibitors are reported.

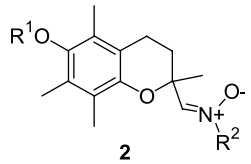


R = H; R_1 = NH_2, $NHCH_2CH_2OH$, $NHCH_2CH_2CH_2OH$, $NHCH_2CH_2NEt_2$, OMe, OCH_2CF_3, $OCH_2CF_2CHF_2$, OCH_2CH_2OH, $OCH_2CH_2NMe_2$
R = CO_2Me; R_1 = NH_2, OMe

Oxazolidinone derivatives containing (un)substituted-benzotriazole ring were synthesized and exhibited potent in vitro antibacterial activity against many antibiotic-resistant microbial strains. Several analogues from this series were comparable or more potent than linezolid in vitro.

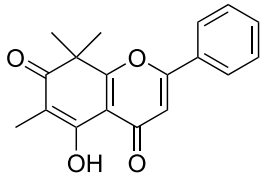
We used structure-based design to develop novel TF/VIIa inhibitors containing a P_1 side pocket moiety that engages Lys192 and Gly216 as demonstrated in an enzyme/inhibitor X-ray crystal structure.



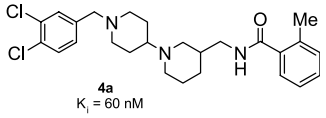


2

Synthesis of nitrone derivatives of trolox **2** is described. Their biological evaluation was performed in vitro for scavenging different free radicals, inhibiting Fe^{2+}-induced lipid peroxidation, and in vivo in a permanent middle cerebral artery occlusion model in mice. New compounds **2** exert pharmacological activities comparable to or better than those of trolox or nitrone-type reference compounds.

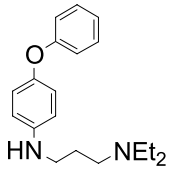


1 Desmosdumotin B

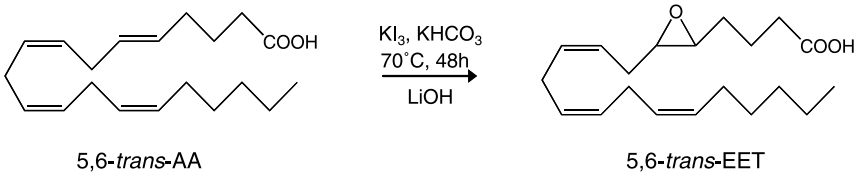


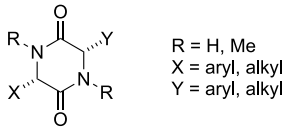
4a
K_i = 60 nM

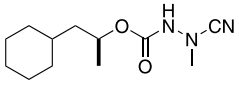
The structure–activity relationship of 3-substituted bipiperidine **4a** as a CCR3 antagonist has been investigated.



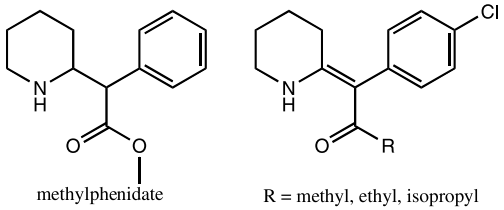
A new series of chemosensitizers against drug resistant and sensitive strains of *P. falciparum* were designed on the basis of a basic chemosensitizing pharmacophore hypothesis.

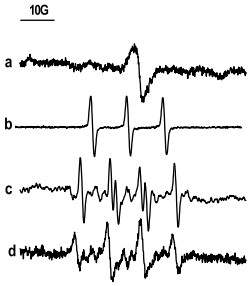


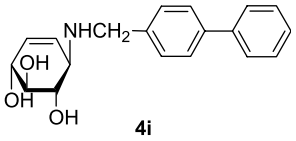




Conversion of the proline-derived cyanamide lead into an acyclic cyanamide capable of forming an additional hydrogen bond with cathepsin K resulted in a large increase in inhibitory activity. An X-ray structure of a co-crystal of a cyanamide with cathepsin K confirmed the enzyme interaction. Furthermore, a representative acyclic cyanamide inhibitor **6r** was able to attenuate bone resorption in the rat calvarial model.

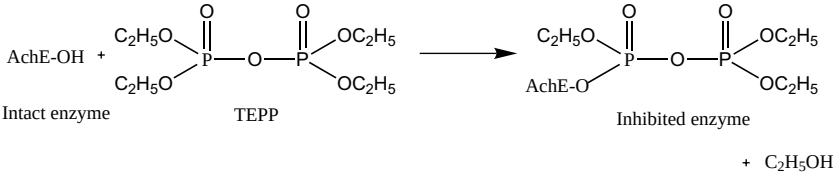


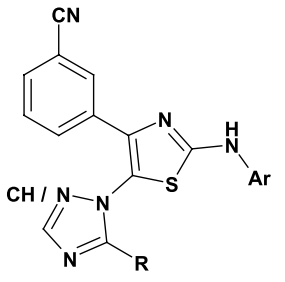


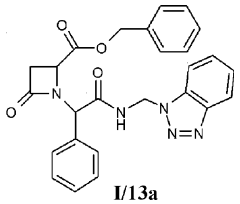


4i

Although conduramine B-1 is not an inhibitor of β-glucosidases, *N*-benzyl derivatives inhibit these enzymes with K_i in low micromolar range. For **4i**: K_i (β-glucosidase from almond) = 8 μM (competitive).

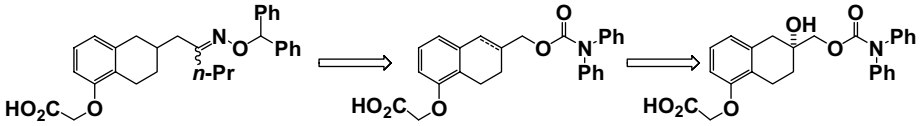






I/13a

Compounds of a combinatorial monocyclic beta-lactam library were found to be apparently uncompetitive inhibitors of HIV-1 protease, providing lead compounds for a new class of HIV protease inhibitors.



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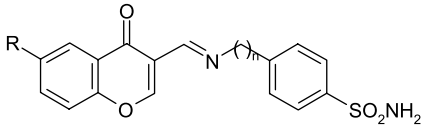
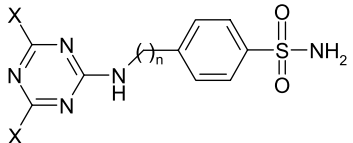
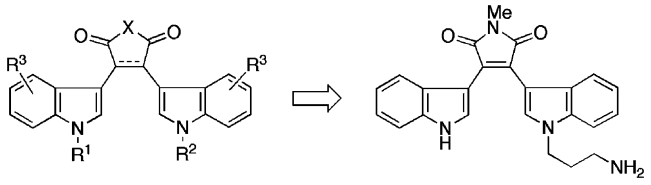


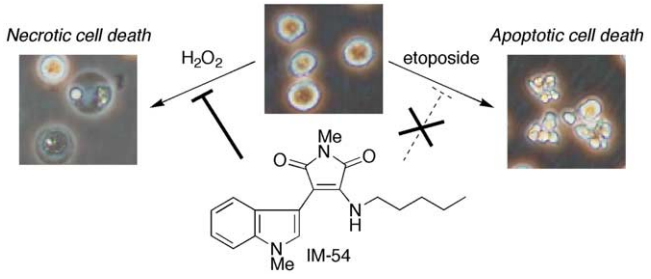
R = H, Me

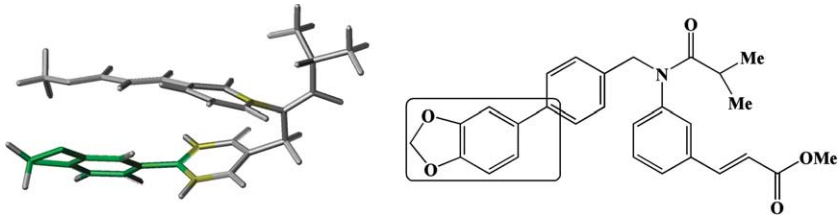


X = NHR, NRR', OPh
n = 0, 1, 2

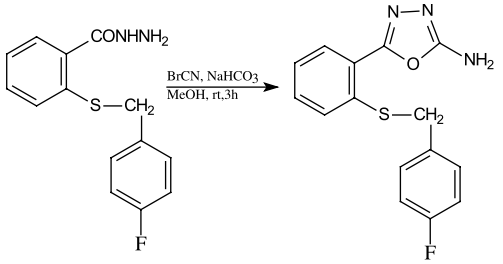


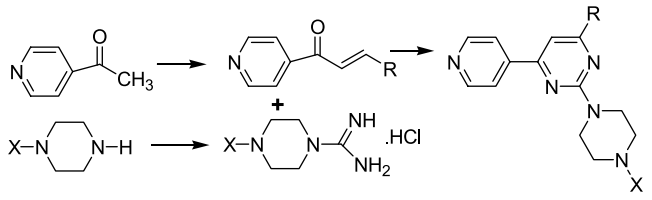
A series of *N*-methyl-bisindolylmaleimide derivatives was synthesized and evaluated as cell death inhibitors.



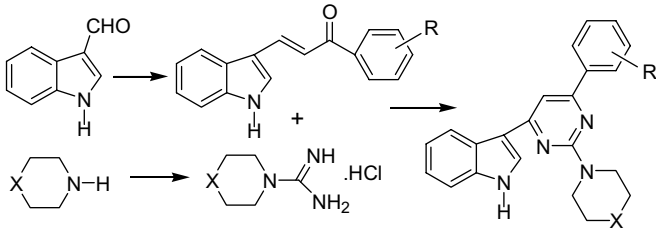


1,3,4-Oxadiazole derivatives were designed and synthesized as benzodiazepine receptor agonists. The pharmacological effect of the synthesized compounds was determined through PTZ and MES tests.

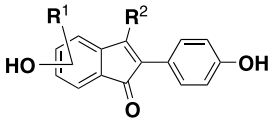


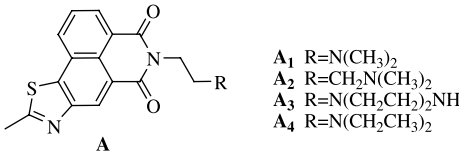


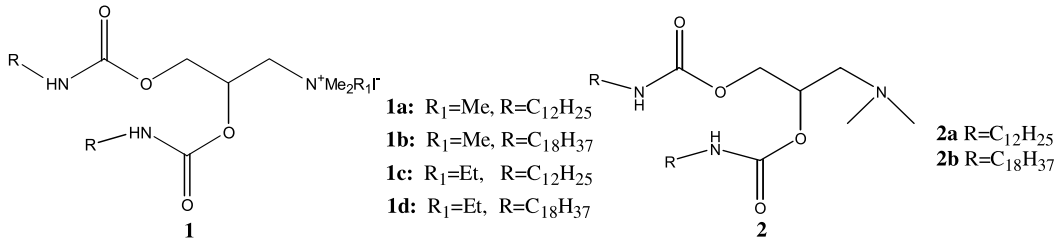
A series of 2,4,6-trisubstituted-pyrimidines was synthesized and evaluated for their in vitro antimalarial activity. Out of the 30 compounds synthesized 21 compounds showed MIC in the range of 0.5–2 μg/mL.



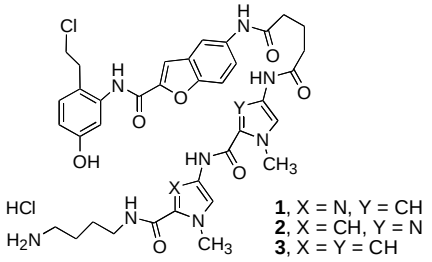
A series of substituted indole derivatives were synthesized and evaluated for their in vitro antimalarial activity against *P. falciparum*. Out of the 24 compounds synthesized six compounds have shown MIC of 1 μg/mL.

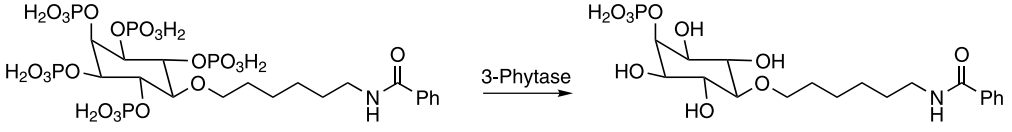


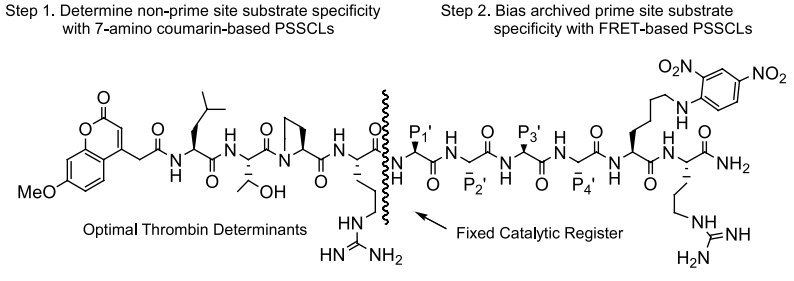




Cationic lipids **1a–d** and neutral lipids **2a**,**b**, with carbamate linkages between hydrocarbon chains and ammonium or tertiary amine head, which were pH sensitive, were synthesized for liposome-mediated gene delivery.







OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

2005: The proteolytic enzyme memapsin 2 (β-secretase, BACE-1) is the protease that cleaves the β-amyloid precursor protein (APP) to produce the 40-42 residue amyloid-β peptide (Aβ) in the human brain, a key event in the progression of Alzheimer's disease (AD). The X-ray crystal structure of memapsin 2 complexed with a peptidomimetic cyclic inhibitor is depicted. Inhibitor (green) is in the binding cleft of memapsin 2 shown as a ribbon diagram for the polypeptide backbone [Ghosh, A. K.; Devasamudram, T.; Hong, L.; DeZutter, C.; Xu, X.; Weerasena, V.; Koelsch, G.; Bilcer, G.; Tang, J. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 15].

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