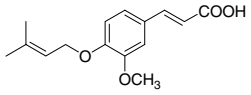
ELSEVIER

Bioorganic &
Medicinal
Chemistry
Letters

Bioorganic & Medicinal Chemistry Letters Vol. 16, No. 21, 2006

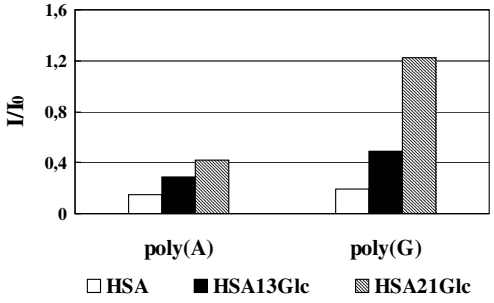
Contents

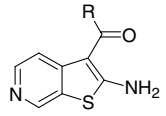
ARTICLES



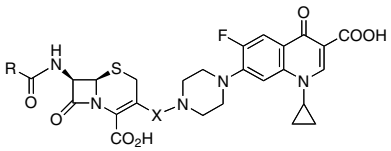
3 MIC= 1.62 μg/mL

The synthesis and the in vitro inhibition of growth of *Helicobacter pylori* of boropinic acid **3**, active principle of *Boronia pinnata*, (MIC = 1.62 μg/mL) and other prenyloxy cinnamic acids and auraptene is reported.

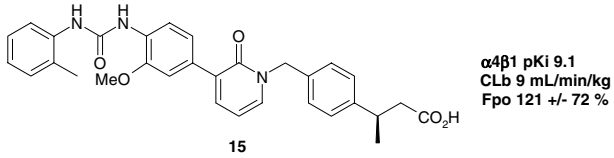




R= substituted phenyl, 1-naphthyl, 2-thienyl

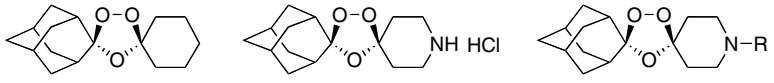


1. X = CH_2 **2**. X = CH_2OCO

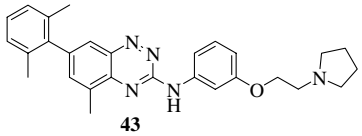


15

Systematic optimisation of a previously described series of novel VLA-4 antagonists has identified a potent orally bioavailable VLA-4 integrin antagonist.

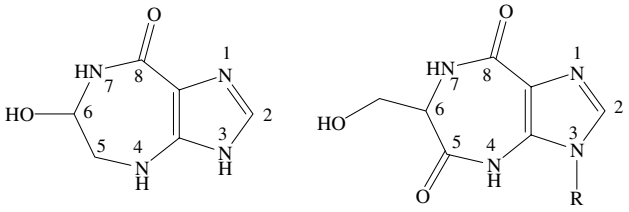


Log P 6.1 Log D 0.25 Log P/D 1.1-5.6



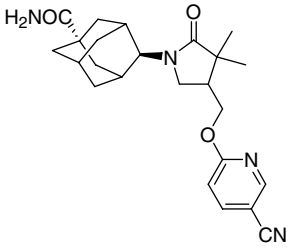
43

We report the SAR studies of a series of structurally novel benzotriazine analogs as inhibitors of Src. The 3-(2-(1-pyrrolidinyl)-ethoxy)phenyl analog (**43**) was identified as one of the most potent inhibitors.

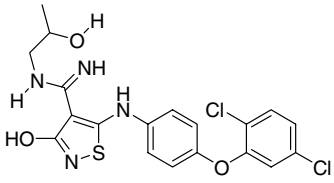


Azepinomycin

1, R = -$CH_2C_6H_5$
2, R = H

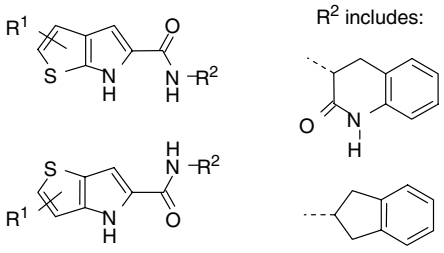


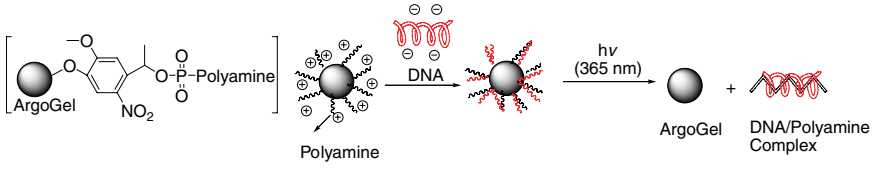
A series of metabolically stable butyrolactam 11β-HSD1 inhibitors have been synthesized and biologically evaluated.



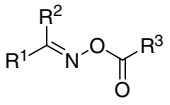
IC50: 28 nM
EC50: 75nM;
Oral AUC: 23908 ng-h/ml

Novel thienopyrrole inhibitors of recombinant human liver glycogen phosphorylase are described, in particular: SAR, hepatocyte activity and binding at the dimer interface site of the rabbit muscle enzyme (X-ray crystallography).

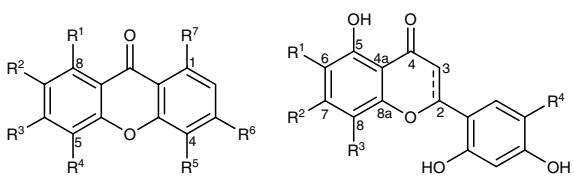




This work describes the synthesis of solid phase with polyamines and DNA binding and controlled release followed by photoirradiation.

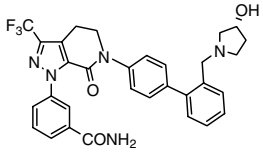


Among the tested oxime derivatives, cyano- and morpholino-substituted analogue **4f** at R^2 and R^3 had the highest potency with an IC_{50} value of 0.05 μM in whole human plasma.

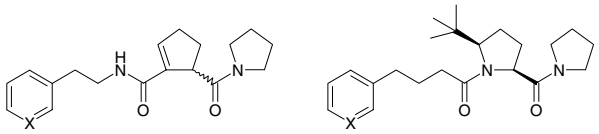


The catecholic xanthones and flavonoids **1**–**13** were isolated from the chloroform extracts of the root bark of *Cudrania tricuspidata*. Compounds **1** and **3**–**8** exhibited significant antioxidant activity against LDL oxidation in TBARS assay. Among them, **10**–**12** showed an inhibitory effect on the NO production and iNOS expression in RAW264.7 cells. Also, compounds **1**, **2**, **5**, **7**, **9**, and **11** preferentially inhibited hACAT-2 than hACAT-1, whereas compounds **3**, **4**, **6**, and **8** showed a similar specificity against hACAT-1 and -2. However, flavonoids **10**, **12**, and **13** dominantly inhibited hACAT-2, not hACAT-1.

The bicyclic tetrahydropyrazolopiperidinone scaffold allowed for the incorporation of multiple neutral P1 moieties with subnanomolar binding affinities for blood coagulation factor Xa. The compound 3-[6-(2′-dimethylaminomethyl-biphenyl-4-yl)-7-oxo-3-trifluoro-methyl-4,5,6,7-tetrahydro-pyrazolo[3,4-*c*]pyridine-1-yl]-benzamide **6d** shows good Xa potency, selectivity, in vivo efficacy, and oral bioavailability. Compound **6d** was selected for further pre-clinical evaluations.

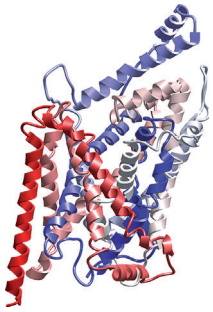


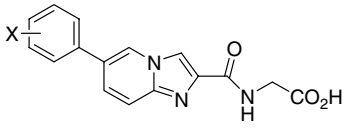
6d

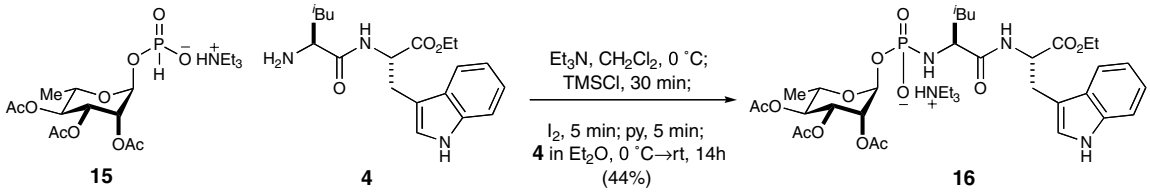


X = C: IC_{50} = 1.5 nM, log P = 1.9
X = N: IC_{50} = 2.2 nM, log P = 0.6

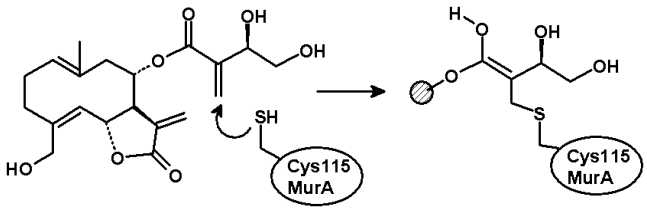
X = C: IC_{50} = 1.2 nM, log P = 3.3
X = N: IC_{50} = 2.1 nM, log P = 2.0



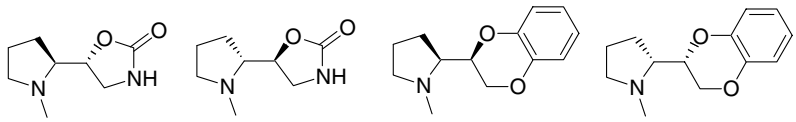


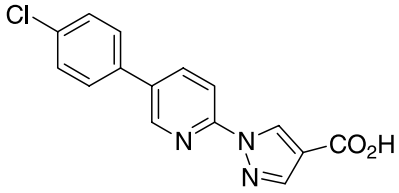


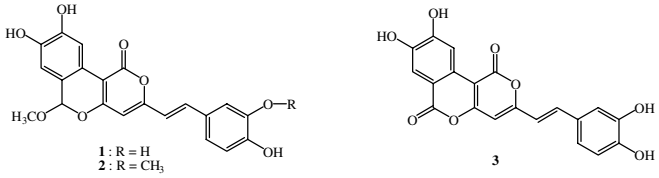
We report the preparation of a phosphoramidon precursor **16** in 44% yield from *H*-phosphonate **15** and H_2N-Leu-Trp-OEt **4**.



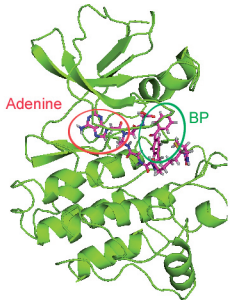
Certain sesquiterpene lactones are potent inhibitors of the antibacterial target enzyme MurA. We present structure–activity relationships and discuss biological implications.



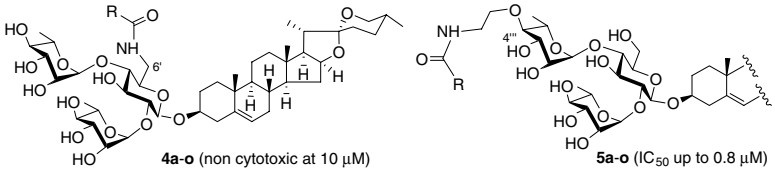


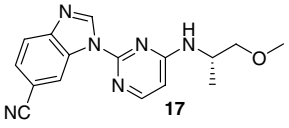


New free radical scavengers **1** and **2** were isolated from the methanolic extract of the fruiting body of the medicinal mushroom *Inonotus xeranticus*, along with the known compounds phelligridin D, 3,4-dihydroxybenzaldehyde, and 3,4-dihydroxybenzoic acid. Their structures were established by extensive spectroscopic data. Compounds **1** and **3** were proposed to be biosynthesized from the oxidative coupling of the precursor hispidin with 3,4-dihydroxybenzaldehyde and 3,4-dihydroxybenzoic acid, respectively. These compounds exhibited significant free radical scavenging activity.



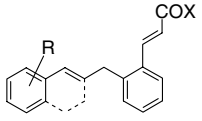
A simple molecular probe containing adenine and benzophenone was found to tag Lck in a highly selective manner.





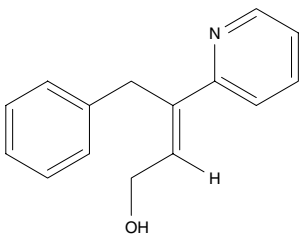
IC50 Jak3/Jak2 =45/145 nM

A new class of pyrimidine-based Janus tyrosine kinase 3 (JAK3) inhibitors are described. Many of these inhibitors showed low nanomolar activity against JAK3.

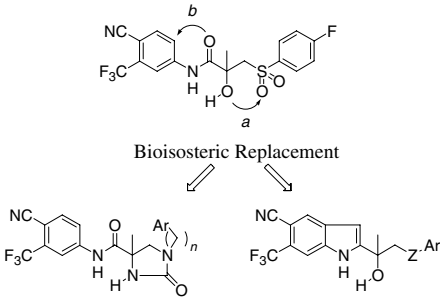


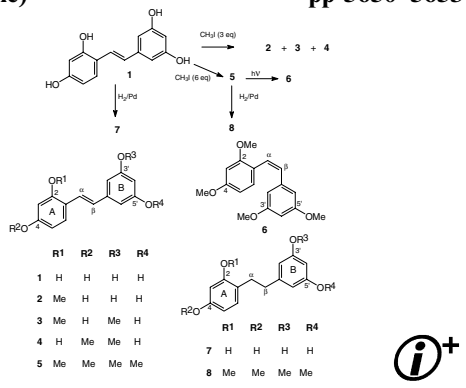
R = H, OBn
X = OH, $NHSO_2Ar$

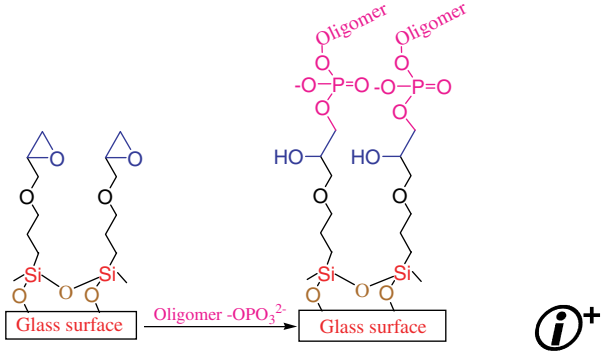
The structural differences and their effects on the biological activity in vivo, in vitro and metabolism have been analyzed.

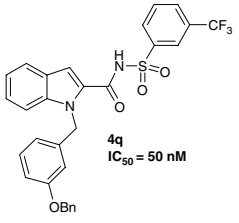


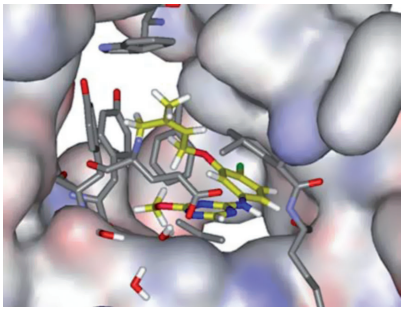
A novel compound, (*E*)-4-phenyl-3-(pyridine-2-yl)but-2-en-1-ol, showing antiproliferative effect is reported.

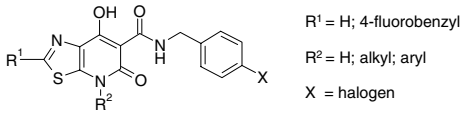




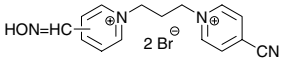




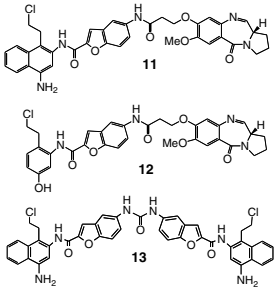


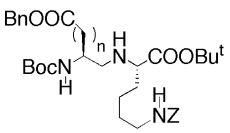


HIV integrase strand transfer IC_{50} range = 151–0.03 μM.

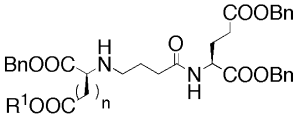


A series of asymmetrical bisquaternary reactivators of acetylcholinesterase (AChE) bearing cyano-moiety with propane connecting chain was synthesized and evaluated on tabun and paraoxon-inhibited AChE with promising results.

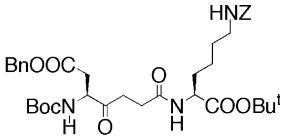




3a n = 1
3b n = 2



8a n = 1, R^1 = Bn
8b n = 2, R^1 = Dmp
8c n = 2, R^1 = *c*Hex



16

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Typical snapshot of **7b** bound to HIV-RT from an MC simulation. Carbon atoms of **7b** are gold; from the left, Tyr181, Tyr188, Phe227, Leu100, Lys101; Trp229 at the top, Val106 at the bottom. H-bond with Lys101 O on right. Some residues in front including Glu138 have been removed for clarity. The water on N5 is also H-bonded to a carboxylate O of Glu138. [Thakur, V. T.; Kim, J. T.; Hamilton, A. D.; Bailey, C. M.; Domaoal, R. A.; Wang, L.; Anderson, K. S.; Jorgensen, W. L. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5664.]

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

ELSEVIER
ISSN 0960-894X