Bioorganic & Medicinal Chemistry 21 (2013) 835–840

Contents lists available at SciVerse ScienceDirect

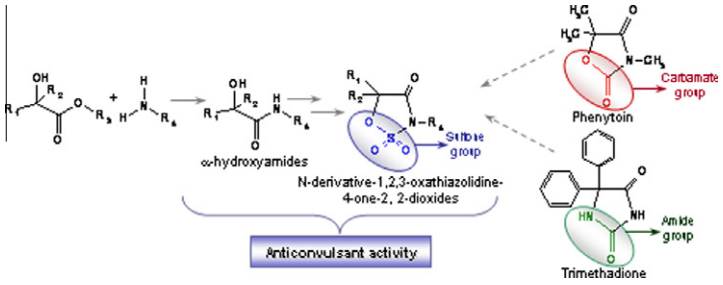
Bioorganic & Medicinal Chemistry

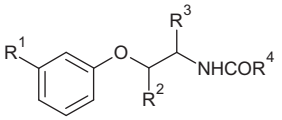
journal homepage: www.elsevier.com/locate/bmc

Bioorganic & Medicinal Chemistry Volume 21, Issue 4, 2013

Contents

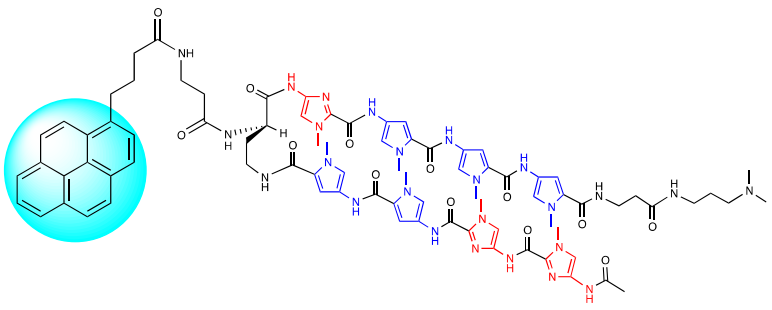
ARTICLES

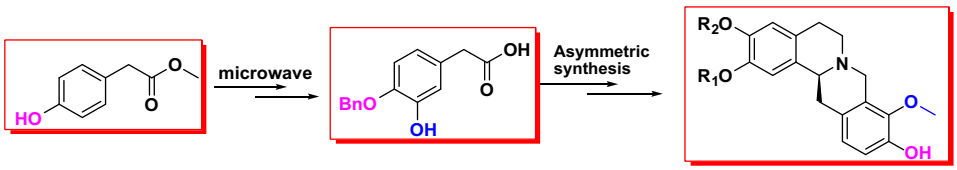




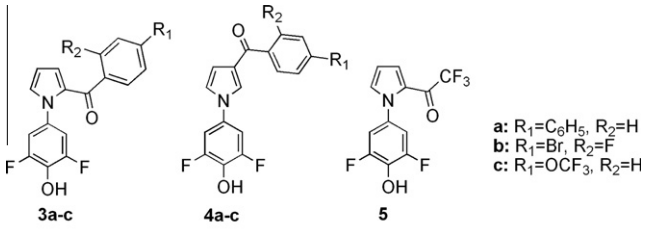
R^1 = H, OMe
R^2, R^3 = H, Me
R^4 = Me, c-Pr, *n*-Pr

The antioxidant properties and the ability to interact with Ca^{2+}/CaM-dependent kinase II of a series of chiral non-indolic melatonergic ligands were investigated.



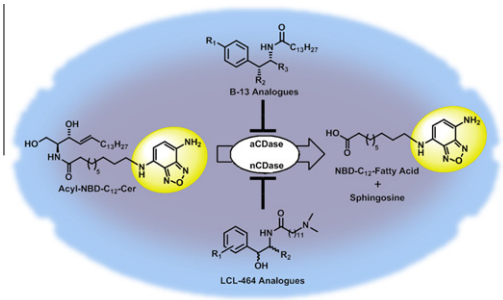


18k: R_1, R_2 = CH_3, CH_3 K_i (5-HT_{1A}) = 149 nM
K_i (D_1) = 50 nM, K_i (D_2) = 305 nM
18m: R_1, R_2 = CH_2 K_i (5-HT_{1A}) = 908 nM
K_i (D_1) = 6.3 nM, K_i (D_2) = 145 nM

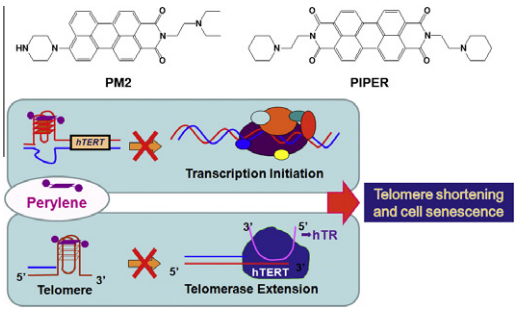


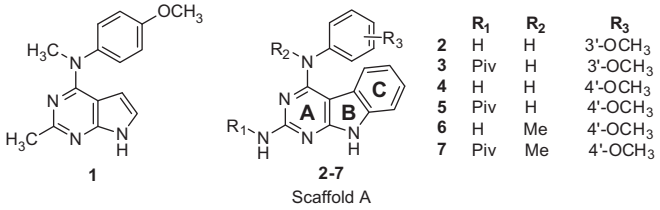
a: R_1=C_6H_5, R_2=H
b: R_1=Br, R_2=F
c: R_1=OCF_3, R_2=H

IC_{50}^{ALR2}=190 nM (3b) $SI^{ALR1/ALR2}$=238 (3a)

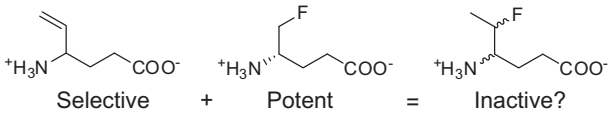


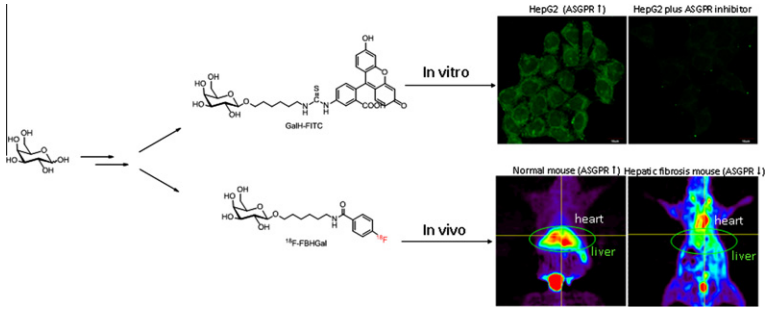
In this study we describe the design and synthesis of a series of modified B-13 and LCL-464 analogues with different substituents as inhibitors of recombinant acid and neutral ceramidases. We show that the inhibition potential of B-13 could be enhanced both in in vitro and in intact cells by suitable modification of functional groups. Furthermore, a detailed SAR investigation on LCL-464 analogues revealed some potent compounds for the inhibition of both aCDase and nCDase with the elevation of ceramide level.

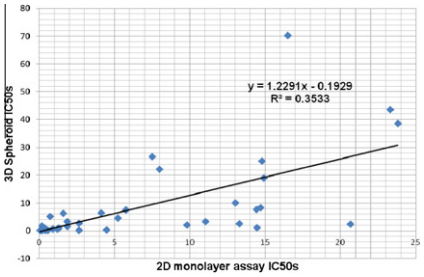


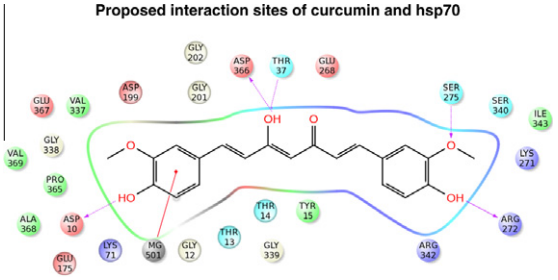


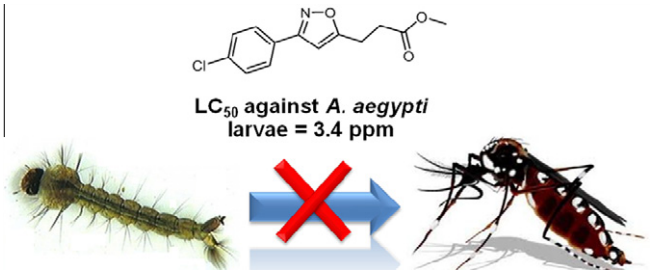
	R_1	R_2	R_3
2	H	H	3'-OCH_3
3	Piv	H	3'-OCH_3
4	H	H	4'-OCH_3
5	Piv	H	4'-OCH_3
6	H	Me	4'-OCH_3
7	Piv	Me	4'-OCH_3

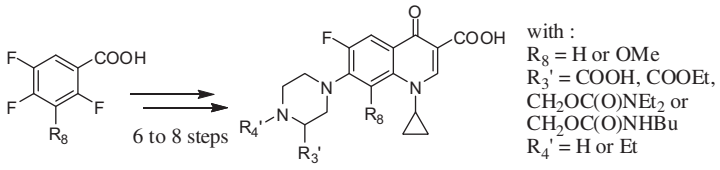


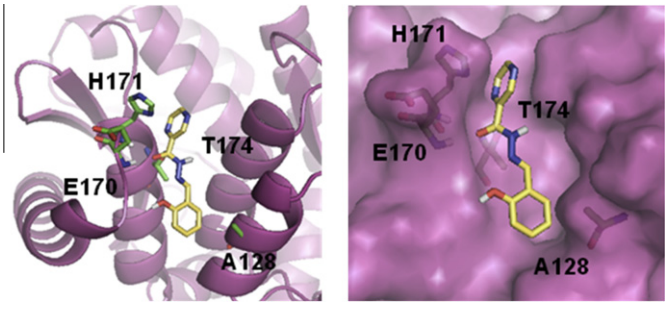


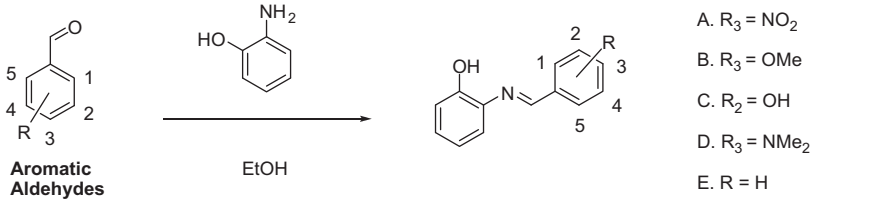


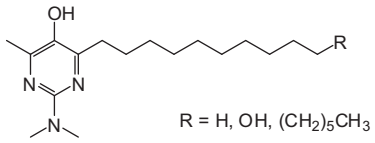


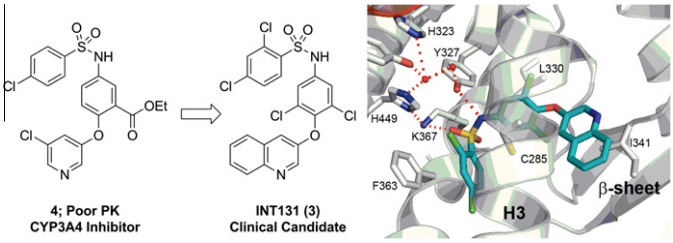


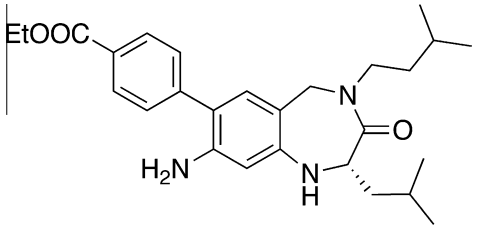


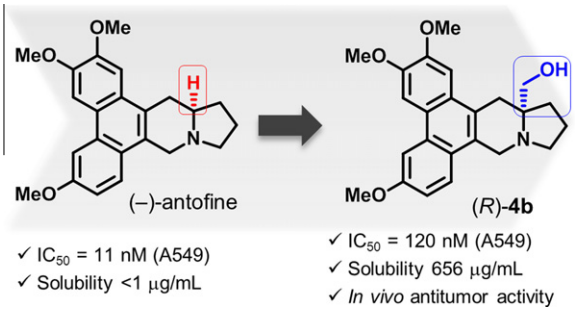


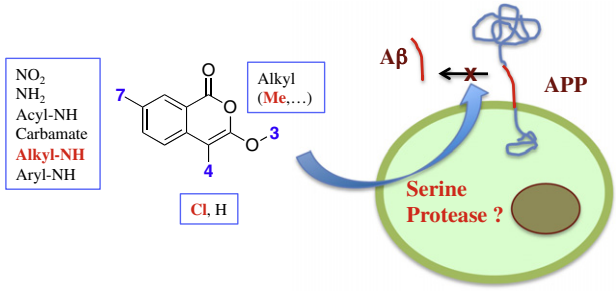












*Corresponding author
Supplementary data available via SciVerse ScienceDirect

COVER

Botulinum neuortoxins are the most lethal toxins known to man and are considered by the Centers for Disease Control and Prevention (CDC) to be a "Category A" agent placing them as one of the six highest priority bioterrorist agents. There are no approved pharmacological treatments for botulinum neurointoxication. The work detailed combines studies using synthesis, crystallography, modeling, kinetic and cellular research to advance pharmacological intervention against this neurotoxin. [Šilhár, P.; Silvaggi, N.R.; Pellett, S.; Čapková, K.; Johnson, E.A; Allen, K.N; Janda, K.D. *Bioorg. Med. Chem.* DOI: 10.1016/j.bmc.2012.12.001]

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. Also covered in the abstract and citation database SciVerse Scopus®. Full text available on SciVerse ScienceDirect®

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ISSN 0968-0896