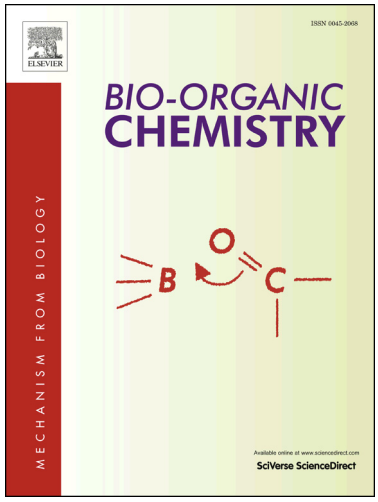

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PII: S0045-2068(16)30409-6
DOI: http://dx.doi.org/10.1016/j.bioorg.2017.02.010
Reference: YBIOO 2020

To appear in: *Bioorganic Chemistry*

Received Date: 12 December 2016
Revised Date: 10 February 2017
Accepted Date: 18 February 2017

Please cite this article as: M. Krátký, S. Štěpánková, K. Vorč áková, L. Navrátilová, F. Trejtnar, J. Stolař íková, J. Vinšová, Synthesis of Readily Available Fluorophenylalanine Derivatives and Investigation of Their Biological Activity, *Bioorganic Chemistry* (2017), doi: http://dx.doi.org/10.1016/j.bioorg.2017.02.010

Synthesis of Readily Available Fluorophenylalanine Derivatives and Investigation of Their Biological Activity

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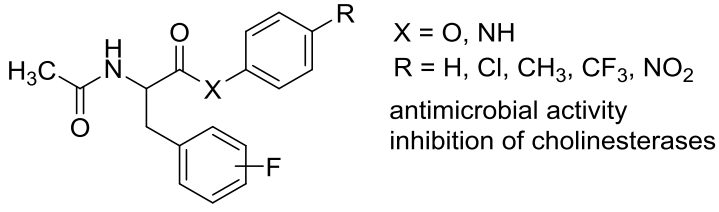
Abstract

A series of thirty novel *N*-acetylated fluorophenylalanine-based aromatic amides and esters was synthesized using *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide or phosphorus trichloride in pyridine. They were characterized by spectral methods and screened against various microbes (*Mycobacterium tuberculosis*, non-tuberculous mycobacteria, other bacteria, fungi), for their inhibition of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) and cytotoxicity. All amino acids derivatives revealed a moderate inhibition of both cholinesterases with IC_{50} values for AChE and BChE of 57.88-130.75 µM and 8.25 to 289.0 µM, respectively. Some derivatives were comparable or superior to rivastigmine, an established drug. Phenyl 2-acetamido-3-(4-fluorophenyl)propanoate was identified as the selective and most potent inhibitor of BChE. The esterification and amidation of parent acids led to an improved BChE inhibition. The esters are better inhibitors of BChE than the amides. The introduction of NO_2 and CH_3 groups into aniline ring and CF_3 moiety in phenol is translated into lower IC_{50} values. Seven compounds showed selectivity index higher than 10 for at least one cholinesterase. Especially the esters exhibited a mild activity against Gram-positive bacteria, mycobacteria and several fungal strains with minimum inhibitory concentrations starting from 125 µM. The highest susceptibility was recorded for *Trichophyton mentagrophytes* fungus.

Graphical Abstract



Keywords