

Accepted Manuscript

Chemoselective synthesis and biological evaluation of arylated 2-(Trifluoromethyl) quinolines as nucleotide pyrophosphatase (NPPs) inhibitors

David Kuhrt, Syeda Abida Ejaz, Saira Afzal, Shafi Ullah Khan, Joanna Lecka, Jean Sévigny, Peter Ehlers, Anke Spannenberg, Jamshed Iqbal, Peter Langer



PII: S0223-5234(17)30539-1

DOI: [10.1016/j.ejmech.2017.07.017](https://doi.org/10.1016/j.ejmech.2017.07.017)

Reference: EJMECH 9580

To appear in: *European Journal of Medicinal Chemistry*

Received Date: 5 May 2017

Revised Date: 27 June 2017

Accepted Date: 11 July 2017

Please cite this article as: D. Kuhrt, S.A. Ejaz, S. Afzal, S.U. Khan, J. Lecka, J. Sévigny, P. Ehlers, A. Spannenberg, J. Iqbal, P. Langer, Chemoselective synthesis and biological evaluation of arylated 2-(Trifluoromethyl) quinolines as nucleotide pyrophosphatase (NPPs) inhibitors, *European Journal of Medicinal Chemistry* (2017), doi: 10.1016/j.ejmech.2017.07.017.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Chemoselective Synthesis and Biological Evaluation of Arylated 2-(Trifluoromethyl)quinolines as Nucleotide Pyrophosphatase (NPPs) Inhibitors

David Kuhrt,^{a,b} Syeda Abida Ejaz,^c Saira Afzal,^c Shafi Ullah Khan,^c Joanna Lecka,^{d,e} Jean Sévigny,^{d,e} Peter Ehlers^{a,b}, Anke Spannenberg,^b Jamshed Iqbal,^c Peter Langer^{a,b,*}

^a *Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, 18059 Rostock, Germany. E-Mail: peter.langer@uni-rostock.de; Fax: +49 381 4986412; Tel: +49 381 4986410*

^b *Leibniz Institut für Katalyse an der Universität Rostock e.V. (LIKAT), Albert-Einstein-Str. 29a, 18059 Rostock, Germany.*

^c *Centre for Advanced Drug Research, COMSATS Institute of Information Technology, Abbottabad, Pakistan*

^d *Département de microbiologie-infectiologie et d'immunologie, Faculté de Médecine, Université Laval, Québec, QC, G1V 0A6, Canada*

^e *Centre de Recherche du CHU de Québec – Université Laval, Québec, QC, G1V 4G2, Canada*

Abstract

A new approach to arylated 2-trifluoromethylquinolines based on novel regioselective Suzuki-Miyaura coupling reactions has been developed. Moreover, site-selective, chemo-selective amination reactions were performed. The new 2-trifluoromethylquinoline derivatives were tested as potential NPPs inhibitors and evaluated for their potential to inhibit two families of ecto-nucleotidases, i.e. NPPs and nucleoside triphosphate diphosphohydrolases (NTPDases). Several derivatives were active on a nanomolar concentration. The results were validated based on docking studies to study the active binding site of the molecules.

Keywords: Palladium catalysis; regioselectivity; quinolines; phosphatase inhibitors

Download English Version:

<https://daneshyari.com/en/article/5158751>

Download Persian Version:

<https://daneshyari.com/article/5158751>

[Daneshyari.com](https://daneshyari.com)