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

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.

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 nanomolecular 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