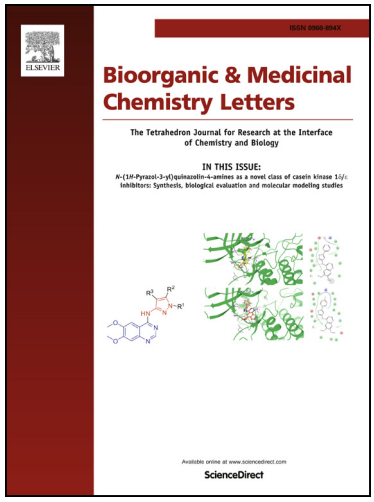
Accepted Manuscript



Lead Selection of Antiparasitic compounds from a focused library of benzene-sulfonyl derivatives of heterocycles

Romina J. Pagliero, Marcel Kaiser, Reto Brun, Marcelo J. Nieto, María R. Mazzieri

PII: S0960-894X(17)30788-6
DOI: http://dx.doi.org/10.1016/j.bmcl.2017.07.081
Reference: BMCL 25194

To appear in: *Bioorganic & Medicinal Chemistry Letters*

Received Date: 22 June 2017
Revised Date: 27 July 2017
Accepted Date: 30 July 2017

Please cite this article as: Pagliero, R.J., Kaiser, M., Brun, R., Nieto, M.J., Mazzieri, M.R., Lead Selection of Antiparasitic compounds from a focused library of benzenesulfonyl derivatives of heterocycles, *Bioorganic & Medicinal Chemistry Letters* (2017), doi: http://dx.doi.org/10.1016/j.bmcl.2017.07.081

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.

ACCEPTED MANUSCRIPT

Lead Selection of Antiparasitic compounds from a focused library of benzenesulfonyl derivatives of heterocycles

Romina J. Pagliero,[a,] Marcel Kaiser,[b,c] Reto Brun,[b,c] Marcelo J. Nieto[d,*] and María R. Mazzieri [a]

[a] *Departamento de Farmacia, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba. Córdoba, Argentina*

[b] *Department Medical Parasitology and Infection Biology, Swiss Tropical Institute, CH-4002 Basel, Switzerland*

[c] *University of Basel, CH-4003 Basel, Switzerland*

[d] *Department of Pharmaceutical Sciences, School of Pharmacy, Southern Illinois University Edwardsville, Campus Box 2000, Edwardsville, Illinois, 62026, USA*

Abstract

A library of 89 synthetic benzenesulfonyl derivatives of heterocycles with drug-like properties was assayed for *in vitro* antiparasitic activity and the results were added to our previously reported derivatives for a comprehensive SAR evaluation. Four compounds showed an IC_{50} between 0.25-3 µM against *Leishmania donovani* and low cytotoxicity. Compound **G{16}** (1-(2,3,5,6-tetramethylphenylsulfonyl)-2-methylindoline), was particularly interesting with an IC_{50} similar to the reference drug miltefosine. Seven compounds showed an IC_{50} below 6µM against *Trypanosoma cruzi*, and three of them (E{**3**}, E{**9**} and G{**3**}) were identified as lead scaffolds for further optimization based on their activity-toxicity profile. Two promising structures (B{**15**} and G{**15**}) showed moderate inhibitory activity against *Plasmodium falciparum*. In general, the presence of a benzenesulfonyl moiety improves the antiparasitic activity of the heterocycles included in this study (with the exception of *Trypanosoma brucei rhodesiense*), validating the criteria used in the selection of the privileged structures and diversification used to generate this library. SAR analysis showed that the presence of lipophilic and electron withdrawing groups were favorable for the antiparasitic activity.

Keywords: antiparasitic activity, benzenesulfonyl, heterocycles, SAR, library compounds.

* Corresponding author. E-mail: mnieto@siue.edu. FAX: +1-618-5145

Download English Version:

https://daneshyari.com/en/article/5155364

Download Persian Version:

https://daneshyari.com/article/5155364

Daneshyari.com