66TH INTERNATIONAL

OPEN READINGS

CONFERENCE FOR STUDENTS OF PHYSICS AND NATURAL SCIENCES

ANNUAL ABSTRACT BOOK | 2023

Vilnius University

VILNIUS UNIVERSITY PRESS

Editors

Martynas Keršys
Šarūnas Mickus

Cover and Interior design
Milda Stancikaitė

Vilnius University Press
9 Saulėtekio Av., III Building, LT-10222 Vilnius
info@leidykla.vu.lt, www.leidykla.vu.lt/en/
www.knygynas.vu.lt, www.journals.vu.lt

Bibliographic information is available
on the Lithuanian Integral Library Information System (LIBIS) portal ibiblioteka.lt.

ISBN 978-609-07-0883-5 (ePDF)

DOI: https://doi.org/10.15388/IOR2023

STUDY OF FORMATION OF 1-ARYL-3*a*,8*b*-DIHYDRO-1*H*-BENZOFURO[2,3-*d*]IMIDAZOLES DURING THE VAN LEUSEN REACTION

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Imidazoles are the 7th most common cyclic structure in pharmaceuticals and can be found in thirty commercially available drugs [1]. Compounds containing an imidazole moiety have been found to exhibit anti-cancer, anti-bacterial, anti-microbial, anti-diabetic, and antioxidant properties [2].

One of the most popular methods of imidazole synthesis is the van Leusen reaction [3]. While synthesizing HSP90 inhibitors using this type of reaction, 1-aryl-3*a*,8*b*-dihydro-1*H*-benzofuro[2,3-*d*]imidazoles were obtained alongside the main products — diarylimidazoles. Compounds containing this new tricyclic moiety have not been reported before.

The 2,3-dihydrofuran moiety is found in many different compounds in nature (e.g., (+)-decursivine, linderol A, caraphenol B and many others [4]) and therefore it is important to find new ways of synthesizing this structure. In nature, the hydrogen atoms of the five-membered ring of dihydrobenzofuran most commonly occur in the *trans* configuration, however, compounds containing the *cis* configuration have also been found. These compounds exhibit anti-HIV, antibacterial, antifungal, antimalarial, anticancer, and anti-inflammatory properties [4].

The objective of this work — to synthesize various 1-aryl-3*a*,8*b*-dihydro-1*H*-benzofuro[2,3-*d*]imidazoles and determine the influence of the substituents on the formation of these compounds.

The starting compounds were prepared from salicylic aldehyde and various anilines. During this work, conditions that would promote the formation of 1-aryl-3*a*,8*b*-dihydro-1*H*-benzofuro[2,3-*d*]imidazoles as the major product of the van Leusen reaction were sought after. Numerous experimental conditions were tested — the reaction was carried out at different temperatures and the influence of various organic as well as inorganic bases and their amounts on the yields of the products, was studied.

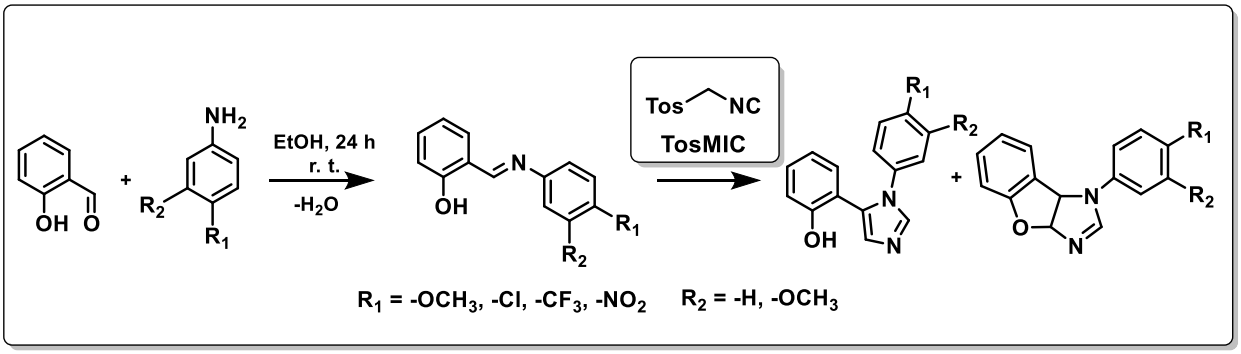

Fig. 1. Condensation of imines as well as the the formation of imidazoles and 1-aryl-3*a*,8*b*-dihydro-1*H*-benzofuro[2,3-*d*]imidazoles in the van Leusen reaction.

The optimal conditions for the formation of 1-aryl-3*a*,8*b*-dihydro-1*H*-benzofuro[2,3-*d*]imidazoles were determined to be MW 40 °C, 5 min and using K_2CO_3 as the base. It was established that the highest yields of 1-aryl-3*a*,8*b*-dihydro-1*H*-benzofuro[2,3-*d*]imidazoles are obtained in aromatic systems with electron withdrawing substituents.

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