UNIVERSITI TEKNOLOGI MARA

SYNTHETIC STUDIES TOWARDS THE TOTAL SYNTHESIS OF QUINOLACTACIN B AND ITS ANALOGUES

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MSc

July 2020

AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

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ABSTRACT

Quinolactacin **1**, was isolated from larvae mulberry pyralid (*Margaronia pyloalis* Welker) It has a unique *N*-methyl-quinolone moiety fused to a lactam ring and was found to contribute towards the activity against tumor necrosis factor production. In this study, a short method on synthesizing quinolactacins and their analogues was established by using 2,4-, and 2,3-pyrrolidinediones as the starting materials. In the first part, 2,4-pyrrolidinedione ring **7** which was also known as tetramic acid underwent amination and acylation reactions to produce two types of key lactam intermediates which are intermediates with enamine functionality (**79** and **11**) and intermediates with enol-ester functionality (**87** and **92)**. The lactam intermediate with enamine functionality, **79** was synthesized from tetramic acid **7** using a stepwise reaction which includes condensation and reduction while enamine **11** was directly synthesized from tetramic acid **7** *via* amination reaction. Lactam intermediates with enol-ester functionality, **87** and **97** were then synthesized from tetramic acid **7** in the presence of sodium hydride in dry THF with different acyl halides which are 2-florobenzoyl chloride and 2-nitrobenzoyl chloride, respectively. The final part focused on synthesizing quinolactacin analogues using 2,3-pyrrolidinedione ring as the starting material. 2,3-Pyrrolidinediones **95**, **96**, and **97** were synthesized *via* a one-pot multicomponent reaction of sodium diethyl oxaloacetate salt, an aldehyde and a primary amine in ethanol. Consequently, 2,3-pyrrolidinedione rings **95**, **96**, and **97** were used to synthesize quinolactacin analogues *via* Conrad limpach reaction which consists of thermal condensation of the primary amine and intramolecular cyclization of enamine intermediates. Despite all the challenges and obstacles in synthesizing quinolactacin B, quinolactacin analogues of **101**, **102**, and **103** were successfully synthesized in short three steps with the yield of 64%, 71% and 70% respectively.

ACKNOWLEDGEMENT

In the name of Allah, The Most Generous, The Most Merciful. Allahamdulillah, upon the completion of my master study, I praise to the almighty Allah for giving me strength, patience and His blessing to complete the study.

I would like to express my sincere gratitude and appreciation to my respectful supervisor, Assoc. Prof. Dr. Zurina Haji Shaameri and my co-supervisor, Prof. Dr. Ahmad Sazali Hamzah for their continuous encouragement, guidance and patience in guiding me to get as much knowledge and experience throughout my study. My sincere thanks also go to Assoc. Prof. Dr. Mohd Fazli Mohammat and Dr. Agustono Wibowo for their advice, suggestion and comments in my research works.

Besides, I would like to thank all the staff of Institute of Science, Mrs Zaleha, Mrs.Afreeda and Mrs. Irmaizatussyehdany for their help in providing the technical assistance. To my fellow labmates Noraishah, Noor Hidayah, Nurul Syafiqah, Nur Aini, Fatin Nur Ain, Muhammad Siddiq, Siti Norazra Khairina, and Muhammad Zulfaqar, special thanks for sharing knowledge, have discussion, giving ideas and comments during the past years. Thank you for all the great moments together.

Finally, this thesis is dedicated to my beloved parents; Mohd Ariff Sulaiman and Siti Aminah Hamzah for their prayers, encouragement and confidence in me to complete this research study and not forgetten to my siblings thank you for the your and support.

Lastly, to those who helped me during my research study either directly or indirectly, thank you so much.

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