UNIVERSITI TEKNOLOGI MARA

STUDIES ON THE SYNTHESES OF SOME NITROGEN HETEROCYCLES WITH A PYRROLIDINE RING SYSTEM

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Thesis submitted in fulfillment of the requirements
for the degree of
Doctor of Philosophy

Faculty of Applied Sciences

JUNE 2007

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 result of my own work, unless otherwise indicated or acknowledged as referenced work. This topic has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

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ABSTRACT

In this study, 3-hydroxy-4-methylproline (Hmp) was chosen as the synthetic target due to its unique structure and its presence in a variety of biologically active natural products.

This thesis has been divided into five main sections. Chapter one is a review of the syntheses of Hmp and its derivatives by different research groups. Chapter two consists of the retrosynthetic analysis of Hmp, whilst chapter three consists of our own synthetic work. Experimental details including the spectroscopic data are provided in chapter four, and finally, future works are recommended in chapter five.

Our synthetic approach towards the synthesis of Hmp involved Dieckmann cyclisation of an intermediate diester, coupled from readily available glycine methyl ester and methyl malonate potassium salt. Dieckmann cyclisation of the diester then gave us the required pyrrolidinone ring template which is also known as the β,β-diketoester. Letting the β,β-diketoester undergo a series of successive chemical reactions, which include alkylation with different electrophiles, stereoselective ketone reduction, demethoxycarbonylation, dialkylation at C-3 position, acylation and alkylation at C-5 position, successfully furnished us with over 40 pyrrolidine type compounds in good to moderate yields. All these attempts were significant to investigate the efficiency of our proposed synthetic route. In this study, we managed to synthesize important intermediates of not only Hmp, **162**, in 5 steps (with an overall yield of 26%) but also an Hmp-derivative, **170**, in 7 steps (with an overall yield of 1.3%). It is also pleasing to note that three of our synthesized compounds were confirmed to exhibit neuroprotective ability *via* the hydrogen peroxide oxidative stress-induced model.

In brief, a novel synthetic approach towards the syntheses of some pyrrolidine type compounds of biological importance was devised. Even though this approach can lead to the synthesis of Hmp, results extracted from this study thus far may be used to develop new scientific knowledge and remarkable findings.

ACKNOWLEDGEMENTS

I would like to thank my supervisor, Professor Dr. Ahmad Sazali Hamzah, for guiding me throughout this research work and especially for all his constructive comments and fruitful suggestions.

I fully appreciate and would like to acknowledge the assistance of all the technical staff involved directly and indirectly in this research project. I am also grateful for the availability of the facilities in the IRDC Science Research Laboratory, Institute of Science as well as Faculty of Applied Sciences.

I would very much like to thank all my friends and colleagues, especially Karimah, Azizah, Suzi, Syed, Salmah and Fazli, in the Organic Synthesis and Natural Products laboratory for their friendship, invaluable assistance and helpful conversation. I would also like to thank my husband, Azmi, for his love and unfailing support, and not forgetting my children, Khairul, Faris, Haziq, Shafiq and Aliyah, for filling my days with laughter and making the difficult times bearable. Most of all, I am very grateful to Allah for blessing me with good health and a lot of patience, without which this work will not be completed.

Finally, I would like to acknowledge Universiti Teknologi MARA for the financial support and for giving me the opportunity to pursue my study.

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