UNIVERSITI TEKNOLOGI MARA

SYNTHETIC STUDIES TOWARDS THE TOTAL SYNTHESIS OF (-)-CODONOPSININE, AN ANTI-HYPERTENSIVE COMPOUND FROM *Codonopsis clematidea*

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

Faculty of Applied Sciences

August 2010

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

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ABSTRACT

In this study (-)-codonopsinine was chosen as the synthetic target molecule due to its unique *trans pentas*ubstituted pyrrolidine structure as well as remarkable antibiotic and hypotensive activity.

The synthetic approach towards the total synthesis of codonopsinine requires an appropriate diketo pyrrolidinone ring template, formed by Dieckmann cyclisation of an intermediate diester which provided the β,β-diketo pyrrolidinone or through condensation with ring closure *via* multicomponent reactions to yield different β,γ-diketo ring template. Performing series of successive functional groups modification on both ring templates, which include demethoxycarbonylation, keto reduction, *O*-protection and β-elimination, successfully furnished over 20 pyrrolidine type compounds in moderate to good yields. In this study, an important intermediate of olefin, **67** was successfully synthesised in 9 steps with an overall yield of 18%. Nevertheless, a different intermediate of acyloins, **82** with completed *N*-Me installation in the ring was also achieved in 3 steps (with an overall yield of 18%) *via* the multicomponent reactions. Biological studies conducted on some of the codonopsinine derivatives confirmed to exhibit from moderate to the most potent activity towards anti-MRSA and efflux pump inhibition.

In brief, two novel synthetic approaches towards the total synthesis of codonopsinine were devised which offer interesting new scientific knowledge and findings.

ACKNOWLEDGEMENT

I would like to thank my supervisor, Professor Dr. Ahmad Sazali Hamzah, for his valuable guidance, philosophical advice, encouragement and support throughout this research project. I am indebted to Associate Professor Dr. Zurina Shaameri for her friendship, constructive comments and proof-reading of my thesis.

I would like to thank all staff of the Institute of Science especially Pn Zaleha Afandi who running the NMR/FTIR and En Shahrizan Miskan for purchasing all the chemicals.

I am grateful to my friends in Organic Synthesis Group especially Dr Yaser, Liyana, Ayu, Kak Pah for their continuous support and humor.

I would like to thank my parents Hj Mohammat Yahya and Hajah for their continuous pray to Allah during the difficult time, my wife Harlina for her sacrifice and my beloved children, Hakim, Zaid, Hassan, Hanis, Yusof, Muslim and Faiz for becoming sunshine in my life.

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

TABLE OF CONTENTS