

**SYNTHESIS OF PYRROLIDINE-2,4-DIONES USING
MELDRUM'S ACID**

FATIN NUR AIN BINTI ABDUL RASHID

**Final Year Project Report Submitted in
Partial Fulfilment of the Requirements for the
Degree of Bachelor of Science (Hons.) Chemistry
in the Faculty of Applied Sciences
Universiti Teknologi MARA**

MAY 2010

ACKNOWLEDGEMENTS

Upon completion of this project, I would like to express my gratitude to many parties.

I would like to express my deep and sincere gratitude to my supervisor, Prof. Dr. Ahmad Sazali Hamzah. His knowledge and his logical way of thinking have been of great value for me. His understanding, encouragement and personal guidance have provided a good basis for the present project.

I wish to express my warm and sincere thanks to En. M. Fazli Mohammat for help detailed review and excellent advice during the progress of this project. I also wish to thank Ms. Zaleha, Ms. Irmaizatussyehdany, and Mr. Shahrizan for their guidance and untiring help during my project.

I owe my loving thanks to my mom and also my dad. Without their encouragement and understanding it would have been impossible for me to finish this project. My special gratitude goes to my siblings for their support.

ABSTRACT

SYNTHESIS OF PYRROLIDINE-2,4-DIONES USING MELDRUM'S ACID

Meldrum's acid is used as a catalyst in the synthesis of pyrrolidine-2,4-diones. The purpose of adding Meldrum's acid into Boc-protected amino acid is to produce an intermediate compound that can further react to produce a five membered ring compound which is Boc-pyrrolidine-2,4-diones. The various types of amino acid are used as the starting material which then are treated with Boc anhydride. Boc anhydride is used to protect the nitrogen group of amino acids and produce Boc-protected amino acids. The Boc-protected amino acids are treated with Meldrum's acid in the presence of DMAP and EDC in DCM. The mixture is refluxed with EtOAc until completion of reaction by TLC. Boc-pyrrolidine-2,4-diones undergo deprotection reaction using strong acid, TFA in DCM to produce pyrrolidine-2,4-diones. The structures of pyrrolidine-2,4-diones were elucidated using modern spectroscopic technique which is nuclear NMR.

TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENTS	iii
TABLE OF CONTENTS	iv
LIST OF TABLE	vi
LIST OF FIGURES	vii
LIST OF SCHEMES	viii
LIST OF ABBREVIATIONS	ix
ABSTRACT	x
ABSTRAK	xi
CHAPTER 1 INTRODUCTION	
1.1 The importance of Pyrrolidine-2,4-diones	1
1.2 The role of Meldrum's acid	3
1.3 Background of study	4
1.3.1 Protection of amino acid	5
1.3.2 Reaction of Boc-amino acid with Meldrum's acid	6
1.3.3 Deprotection of Boc-amino acid	8
1.4 Objectives of the research	9
1.5 Significance of study	9
1.6 Problem statement	9
CHAPTER 2 LITERATURE REVIEW	
2.1 Synthesis of tetramic acid	10
2.2 Synthesis of chiral cyclic statines	11
2.3 Synthesis of pyrrolidine-2,4-diones	12
2.4 Synthesis of <i>N</i> -alkoxycarbonyl-3-substituted tetramic acids	13
2.5 Meldrum's acid and related compounds in the synthesis of natural products and analogs	14

CHAPTER 1

INTRODUCTION

1.1 The importance of Pyrrolidine-2,4-diones

N-Acylated pyrrolidine-2,4-diones (also known as *N*-acylated tetramic acids) are integral part of a number of physiologically active natural products (Anastasia Detsi *et al.* 1998).

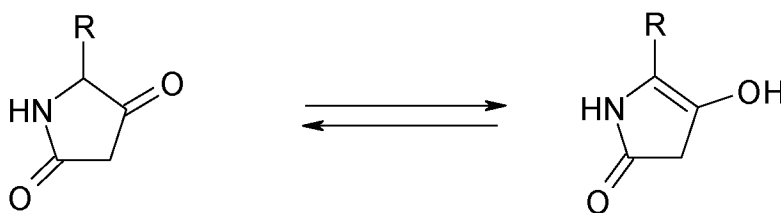


Figure 1.1 Keto-enol tautomerisation in tetramic acid

Many of the natural products displayed some interesting biological activities such as antibiotic, antiviral, or cytotoxic activities. The structure of the pyrrolidine-2,4-diones is closely related to that of amino acids, and the biosynthetic pathway has indeed been suggested to occur *via* an intramolecular condensation of *N*-acetyl amino acid methyl esters (Masood Hosseini *et al.* 2006).