

**SYNTHESIS AND DECARBOXYLATION OF BENZYLATED  
 $\beta,\beta$ -DIKETOESTER TOWARDS THE SYNTHESIS OF PREUSSIN**

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## TABLE OF CONTENTS

<b>ACKNOWLEDGEMENTS</b>	<b>Page</b>
	iii
<b>TABLE OF CONTENTS</b>	iv
<b>LIST OF FIGURES</b>	vii
<b>LIST OF SCHEMES</b>	viii
<b>LIST OF ABBREVIATIONS</b>	ix
<b>ABSTRACT</b>	xi
<b>ABSTRAK</b>	xii

### CHAPTER 1: INTRODUCTION

1.1	Biologically relevant compounds: Nitrogen heterocycles	1
1.2	Background of preussin	3
1.3	Scope of study	4
	1.3.1 Esterification reaction	4
	1.3.2 Condensation reaction	4
	1.3.3 Dieckmann cyclization reaction	5
	1.3.4 Decarboxylation reaction	5
1.4	Significance of study	6
1.5	Objectives of study	6
1.6	Proposed retrosynthetic strategy for the synthesis of preussin	8

### CHAPTER 2: LITERATURE REVIEW

2.1	Previous study on esterification reaction	9
	2.1.1 Esterification of aromatic carboxylic acids	9
2.2	Previous study on condensation reaction	10
	2.2.1 Condensation of benzyl malonyl chloride with <i>N</i> -benzyl glycine ethyl ester	10
	2.2.2 Coupling of glycine methyl ester with methyl malonate potassium salt	11
	2.2.3 Condensation of 1-allylpyrrolidine-2,3-dione with 2-aminobenzaldehyde	12
2.3	Previous study on Dieckmann cyclization reaction	13
	2.3.1 Dieckmann cyclization of <i>N</i> -benzyl- <i>N</i> -ethoxycarbonylmethyl-malonamic acid benzyl ester	13
	2.3.2 Dieckmann cyclization of <i>N</i> -methoxycarbonylmethyl-malonamic acid methyl ester	14
2.4	Previous study on decarboxylation reaction	15
	2.4.1 Refluxing of 1-isopropyl-2-oxo-cyclohexanecarboxylic acid ethyl	15

## ABSTRACT

### **SYNTHESIS AND DECARBOXYLATION OF BENZYLATED $\beta,\beta$ -DIKETOESTER TOWARDS THE SYNTHESIS OF PREUSSIN**

This thesis describes a simple and efficient methodology for the synthesis and decarboxylation of benzylated  $\beta,\beta$ -diketoester, 5-benzyl-2,4-dioxopyrrolidine-3-carboxylate towards the synthesis of preussin. Preussin is a pyrrolidinol alkaloid which originally understood to have significant antifungal activity. Preussin therefore provide an interesting lead structure for the design of novel antitumor drugs. Thus, in this synthesis, the key compound, 5-benzyl-pyrrolidine-2,4-dione was synthesis by a few effective steps. The initial step was the esterification to produce a product that can be coupled with methyl malonate potassium salt. The product from the coupling was then cyclized to obtain the  $\beta,\beta$ -diketoester mentioned. Lastly, decarboxylation step was performed to remove the ester group, thus, producing the key compound towards the synthesis of preussin. All products synthesized were purified and then characterized using FTIR,  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  spectroscopy for structure confirmation.

# CHAPTER 1

## INTRODUCTION

### 1.1 Biologically Relevant Compounds : Nitrogen Heterocycles

Heteroatoms (*hetero*, “different”) are any atoms other than carbon and hydrogen. Heterocyclic compounds, or heterocycles, are cyclic compounds in which one or more of the atoms of the rings are heteroatoms. Other atoms besides carbon, C, such as N, O, S, Se, P, Si, B and As can be incorporated into the ring structures (Wade, 2003).

Pyrrolidine, also known as tetrahydropyrrole, is an organic compound with the molecular formula  $C_4H_9N$ . It is a cyclic amine with a five-membered ring containing four carbon atoms and one nitrogen atom. It is a clear liquid with an unpleasant ammonia-like odour. Pyrrolidine is found naturally in the leaves of tobacco and carrot. The pyrrolidine ring structure is present in numerous natural alkaloids such as nicotine and hygrine. It is found in many pharmaceutical drugs such as procyclidine and bepridil. It also forms the basis for the racetam compounds, for example, aniracetam and piracetam (<http://www.freebase.com/view/en/pyrrolidine>).

Pyrrolidine and piperidine nitrogen heterocycles occur widely in nature as components of pyrrolizidine, indolizidine and quinolizidine alkaloids and are of considerable biochemical, pharmaceutical and agricultural importance because of their diverse biological activities. Their toxicity and hallucinatory activities are well known, but probably more important are their antibiotic, antibacterial, antifungal and