UNIVERSITI TEKNOLOGI MARA

SYNTHETIC STUDIES TOWARDS THE TOTAL SYNTHESIS OF RIGIDIUSCULAMIDE D: PYRROLIDINONES FROM ASCOMYCETES FUNGUS

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ABSTRACT

The synthetic studies towards the total synthesis of rigidiusculamide D: pyrrolidinone from ascomycetes fungus employed convergent approach was divided into two parts. The first part which was the preparation of tetramic acid ring was then divided into several routes to produce four different compounds of tetramic acid ring. For the first route, methyl acetoacetate was used as the starting material which undergoes alkylation, bromination and intramolecular cyclization reaction which produced two different compounds which were monomethylated compound and dialkylated compound at C3-position of the tetramic acid ring. For the second route, glycine methyl ester, ethyl bromoacetate and sarcosine were used as the starting material which produced unprotected, *N*-benzylated and *N*-methylated tetramic acid ring through alkylation, condensation and Dieckmann cyclization reaction. In the second part, benzofuran ring was synthesized using two different starting materials namely methyl 4-hydroxybenzoate and 4-hydroxybenzaldehyde. Both starting material undergo prenylation reaction, epoxidation and cyclization reaction in order to obtain the target molecules. Finally, after successfully synthesized both desired tetramic acid ring and benzofuran ring, coupling reaction or condensation reaction took place in order to obtain the key carbon skeleton towards the synthesis of rigidiusculamide D: pyrrolidinone.

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CHAPTER ONE
INTRODUCTION

1.1 NATURAL PRODUCTS AS A POTENTIAL SOURCE FOR DRUG DISCOVERY

In the past century, varieties of classes of natural products have been isolated and the characterization of their structure was done for example antibacterial, antifungal and antiviral agents. These discoveries have been the central to the work of organic and medicinal chemist along with the elucidation of biological and biochemical mechanisms of therapeutic action. Natural products have been valuable as tools for developing front-line drugs (David J. Newman, Gordon M. Cragg, and Kenneth M. Snader, 2000). However, the scope for making chemical modifications to optimize their therapeutic application can be limited by the complexity of many natural products (David J. Newman, Gordon M. Cragg, Susan Holbeck, and Edward A. Sausville, 2002). Moreover, it can be problematic to acquire a renewable supply of active compounds from biological sources. Therefore, studies on natural products syntheses among the preliminary steps to overcome the scarcity of these natural products resources.

In many bioactive natural products such as tetramic acid (pyrrolidin-2,4-diones), azasugars, and γ-hydroxy- γ-lactams, the key structural features is oxygenated pyrrolidines. The bioactivity of the hydroxylated pyrrolidin-2-ones has captured much interest from organic chemists although they are not yet known as distinct class of natural products.