UNIVERSITI TEKNOLOGI MARA

SYNTHESIS OF PEPTIDES BASED ON BETULINIC ACID SCAFFOLD AND BETULINIC-BUTYROLACTONE DERIVATIVES

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ABSTRACT

Several Betulinic acid peptides here synthesized by incorporating BA with neutral amino acids using standard coupling protocols in the presence of HoBt, HBtu and DiPEA. In addition enantiopure betulinic-acid- cyclohexene silyl ether peptides was successly synthesized in a good yield. Futher olefinic cleavage reaction, afforded betulinic acid -γ- butylrolactone peptides, which undergoes benzylation reaction to furnish desired end product benzylated BA-γ-butylrolactone product. Five new synthesized betulinic acid derivatives were tested for their in vitro cytotoxicity against human corrected carainoma cell lines (HT116). The result of preliminary biological activities showed that three compounds betulinic acid-cyclohexene silyl ether peptides, benzylated betulinic acid-alanine peptide, and benzylated betulinic acid-γ-butylrolactone peptides with more hydrosolubility compare to betulinic acid, possessed impressive cytotoxicity with the IC_{50} values of 50.00, 36.67, 25.33 (μg/ml) respectively

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CHAPTER ONE
INTRODUCTION

1.1 RESEARCH BACKGROUND

There are many reasons why chemists create new organic substances. They may be synthesized as part of research or to demonstrate a new type of reaction, or if a compound is needed with specific chemical and physical properties. Large amounts of some synthetic compounds are routinely produced industrially. Organic chemists can design and create synthetic replicas of naturally produced compounds by adding or removing key functional groups to or from available molecules.

Over the course of the past hundred years, a very large number of syntheses for a wide variety of compounds have been recorded. For all but the simplest of these, a majority of the reactions in the synthesis involve functional group modification, preceding or following a smaller number of carbon-carbon bond forming reactions. In addition reactive functional group in one molecule can be transformed by additions; elimination and substitution inter conversions reactions.

Each step of a synthesis involves a chemical reaction, reagents and conditions for each of these reactions must be designed to give an adequate yield of pure product, with shortest reaction pathway. A method may already exist in the literature for synthesizing one of the early synthetic intermediates, and this method will usually be used rather than an effort to "reinvent the wheel". However, most intermediates are compounds that have never been synthesized before, and these will normally be synthesized using general methods developed by organic chemists. To be useful, these methods need to give high yields, good purity and to be reliable for a broad range of substrates.

For practical applications, additional hurdles include industrial standards of safety and purity. Methodology research usually involves three main stages: discovery, optimisation, and studies of scope and limitations. The discovery requires extensive knowledge of and experience with chemical reactivity of appropriate reagents.