



UNIVERSITI
TEKNOLOGI
MARA

THE DOCTORAL RESEARCH ABSTRACTS

Volume: 10, Issue 10 October 2016

TENTH
ISSUE

INSTITUTE of GRADUATE STUDIES

IGS Biannual Publication



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Title : SYNTHETIC STUDIES TOWARDS THE TOTAL SYNTHESIS OF ZOPFIELLAMIDE A

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In this study, Zopfiellamide A was chosen as a target molecule due to its unique structure and its pharmacological importance. The synthetic strategy moving towards the synthesis of Zopfiellamide A was divided accordingly based on the C-5 and C-3 substitution groups. The first approach was focused on the insertion of C-5 substituents of Zopfiellamide A which is the construction of the quaternary carbon bearing the hydroxyl, isopropyl and carboxylic acid linked *via* the methylene group at C-5 position of the pyrrolidinone ring. Therefore, the C-3 position of the pyrrolidinone ring was protected by a methyl group. Methyl acetoacetate was dialkylated, brominated and cyclised with methylamine to form the required lactam skeleton. The synthesis of C-5 substituents involved olefination, Michael addition, alkylation and mono-decarboxylation to give decarboxylated product **30**, which is closest to the target molecule **12**. There were two more steps left, which are α -hydroxylation and hydrolysis of ester. The overall yield of reaction was about 30%. Meanwhile, the C-acylation on C-3 was done by preparing the studied template of pyrrolidine-2,4-dione template **38**, *via* condensation, dieckmann cyclisation and decarboxylation reaction. The C-acylation reaction was performed using readily available acid

chlorides including crotonyl, benzoyl, naphthoyl, cinnamoyl, and furoyl chloride respectively. The reaction was carried out using strong and weak base, however, the product yield was very low, ranging from 1 to 14% yield to a complex mixture. Meanwhile, the chemical exploration of the pyrrolidinone intermediates produced during the reaction was also done using epoxidation, acid-catalyzed ring-opening and stereoselective reduction. The epoxidation of alkene **17** with mCPBA managed to give epoxide **31**, and treatment with diluted acid was successfully gave diols **32**. The reduction of alkene **17** with sodium borohydride in the presence of CaCl_2 and MnCl_2 was resulted in chemoselective but not stereoselective reaction. However, reduction with sodium borohydride in the presence of MgCl_2 and ZnCl_2 was found to be a chemoselective and stereoselective reaction. The reduction of Michael adduct **19** was successfully resulted in keto reduction and gave compound **35**.