UNIVERSITI TEKNOLOGY MARA

SYNTHESIS AND CHEMICAL EXPLORATION OF NOVEL PYRANO[2,3-C]PYRAZOLE-3-CARBOXYLATE AND ITS DERIVATIVE VIA ONE-POT REACTION

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Thesis submitted in fulfillment
of the requirements for the degree of
Master of Science

Faculty of Applied Sciences

January 2019

ABSTRACT

A simple and green approach for the synthesis of fusedpyrano[2,3-*c*]pyrazole-3-carboxylate and spiropyrano[2,3-*c*]pyrazole-3-carboxylate derivatives was developed. The synthesis was achieved under the optimized condition of domino one-pot, four-component reaction of diethyl oxaloacetate, hydrazine hydrate, aldehyde or ketones and malanonitrile in refluxing acidic ethanolic solution under non-catalytic system. As the results, the desired compound was obtained in relatively high yield which is 82% yields. In order to extend the scope of study, the derivatives of hydrazine hydrate, cyano ester and diketo compound were used to obtain a new class of pyrano[2,3-*c*]pyrazole-3-carboxylate derivatives. This procedure displayed high regioselectivity, furnished generally moderate to excellent yields (70-90% yield) and used easily access starting materials, and displayed operational simplicity. This four-component reaction presumably proceeds via sequential reactions of pyrazole synthesis, Micheal addition and Thorpe-Ziegler cyclization reaction. By having pyrano[2,3-*c*]pyrazole-3-carboxylate in hands, a chemical exploration on the aminonitrile side of the compounds was done by specifically focus on the ring extension for multicyclic compounds through C-C and C-S ring extension. At the end of this study, a total of 30 derivatives which some are new were successfully synthesized.

ACKNOWLEDGEMENT

In completing this project, I would like to express my appreciation to all who assist me especially to Allah S.W.T for giving me the best health, extraordinary tirelessness, effortlessness in doing everything and splendour as a primary concern and soul throughout progressing this project.

At this point, i want to amplify my gratitude towards my supervisor, Dr Mohd Fazli Mohammat @ M Yahya for shrouded direction, counsel and cause for me to finish this project. I would like to thank my co-supervisor, Prof. Dr. Ahmad Sazali Hamzah for his guidance, constructive comments and suggestions. I am indepted to Dr. Zurina Shaameri for his precious advice and inspired me to see things positively.

I fully appreciate and would like to thank all technical support in the Institute of Science especially Mrs. Zaleha, Mrs. Irmaizatussyehdany, Dr Agustono and Mrs Afreeda for their kindness and help. My sincere thanks to all my friends and colleagues for their continuous support and cheerfulness especially Faezuan, Ashraf, Hasliza, Fatin, and all members of Organic Synthesis Laboratory. Thank you for the great moments that we have shared tohether.

Last but not least, i also wanted to show my appreciation towards my parents, En Maarop bin Ishak and as they always support and encourage me physically and mentally.

Finally, I would like to acknowledge Universiti Teknologi MARA for the financial support and for giving me the opportunity to pursue my study.

TABLE OF CONTENTS

CHAPTER ONE
INTRODUCTION

1.1. GREEN CHEMISTRY AND ONE-POT REACTIONS

Sustainable and Green Chemistry in very simple term is a different and sustainable way about how chemistry and chemical engineering can be done. It also can be defined as the design of chemical products and processes that reduce or eliminate the use or generation of hazardous substances. Over the years, different principles have been proposed that can be used when performing the design, development and implementation of the chemical product and process. These principles enable scientist to find a new ways to reduce waste, conserve energy, and discover replacement of less hazardous substance. In 1998, Paul Anastas and John C. Warner authored the groundbreaking book, titled as "Green Chemistry: Theory and Practice" whereby they had outlined 12 principles of Green Chemistry which to motivate academic and industrial scientist towards the green chemistry movement [1]. Since then, chemist had explored ways to apply the green chemistry principle in their research work. In modern days of organic chemistry, efficiency and environmental sustainability are the main issues in order to fulfill the green chemistry principle. Both of these issues need to be discussed thoroughly when making a valuable target molecule over several distinct steps. As a result, chemist had come out with an effective approach to synthesize the target molecule in a single vessel. This approach is often called as one-pot reaction or multi-component reactions. There are some terms to describe the multi-component reaction or one-pot reaction in organic chemistry. These are domino reaction, cascade reaction or tandem reaction [2]. This method is effective because several chemical transformation and bond-forming steps can be carried out in a single pot without producing much side product. Furthermore, this method circumvents several purification steps and thus minimizes chemical waste and save time. It is noteworthy that this multi-component reaction are environmentally benign processes as they follow the green chemistry principle on the basis of waste elimination and avoiding time-consuming purification or protection/deprotection steps [2].