SYNTHESIS AND BIOASSAY STUDIES OF BENZOXAZIN-4-ONE AND QUINAZOLIN-4-IMINE DERIVATIVES

Ng Choon Meng and Joazaizulfazli Jamalis
Department of Chemistry, Faculty of Science, Universiti Teknologi Malaysia, 81310 Johor Bahru.

Abstract

The 4*H*-3,1-benzoxazin-4-one and quinazolin-4-imine derivatives have been synthesized in simple and one step reaction. The reaction of anthranilic acid and benzoyl chloride, terephtaloyl dichloride and 4-chlorobenzoyl chloride in pyridine yielded 2-phenyl-4*H*-3,1-benzoxazin-4-one (78.91%), 1,4-(di-4*H*-3,1-benzoxazin-4-one)benzene (55.23%) and 2-(*p*-chlorophenyl)-4*H*-3,1,-benzoxazine-4-one (33.20%) respectively. The benzoxazin-4-one derivatives were then treated with hydrazine hydrate in absolute ethanol to form 2-phenylquinazolin-4-imine (70.90%), 1,4-(diquinazolin-4-imine)benzene (43.70%) and 2-(*p*-chlorophenyl)quinazolin-4-imine (35.81%). The resulting compounds were characterized using ATR and ^{1}H NMR using $CDCl_3$ as solvent. From both spectra it showed that the synthesis of targeted compound, 4*H*-3,1-quinzolin-4-one was unsuccessful. The resulting compounds after treated with hydrazine hydrate were proposed to be quinazolin-4-imine compounds based on the data analyzed from ATR and ^{1}H NMR spectrum. Antioxidant test using DPPH free radical scavenging has been carried out on the six compounds synthesized. The results showed that 4*H*-3,1-benzoxazin-4-one derivatives did not show antioxidant activity while the compounds of quinazolin-4-imine derivatives showed good antioxidant activity as the IC_{50} value obtained are lower than positive control of ascorbic acid except for 1,4-(diquinazolin-4-imine)benzene. Among the quinazolin-4-imine derivatives, 2-phenylquinazolin-4-imine showed the highest antioxidant activity at IC_{50} value at 2.66ppm. The introducing of electron withdrawing group at phenyl substituent was found to reduce ability of compounds in antioxidant activity.

Keywords: Heterocycle, synthesis, 4*H*-3,1-benzoxazin-4-one, quinazolin-4-imine, antioxidant

INTRODUCTION

Benzoxazinone belongs to the group of heterocyclic compounds that consist of unsaturated six-membered rings with two heteroatoms of oxygen and nitrogen. While the quinazoline consist of unsaturated six-membered rings with two heteroatoms of nitrogen. Heterocyclic compounds are commonly become an interest in pharmaceuticals and agrochemical industries due to their natural occurrence [1]. Numerous additives and dyes used in industrial application such as cosmetic are heterocyclic in nature. The common biological activities possessed by synthetic heterocyclic compounds are antibacterial [2], antifungal [3], anti-inflammatory [4] and antioxidant [5].The wide range of biological activities possessed by heterocycles is mainly due to the extraordinary wide range of reaction of the compounds. Heterocyclic can behave as either acid or base to form anion or cation depending on the pH value of the medium. Besides, some heterocyclic easily interact with electrophilic reagent while some with nucleophiles, or both. Some can be easily oxidized but reduction resistant, or vice versa. Furthermore, there are heterocyclic compounds which simultaneously demonstrate all of the mentioned properties.

Benzoxazinone can exist in various types depends on the position of keto group. The keto group may occur ateither position two, four or both [6].The keto group also may occurat position three of the structure such as natural occurring of benzoxazinone in maize and wheat [7]. Among all the types of benzoxazinone and quinaozoline, 4(3*H*)-benzoxazinone and quinazolinone are more prevalent to be used as intermediates of drugs synthesis or as natural products in biosynthetic pathway. This is partly because of its structure possess wide range of reaction and being derived from anthranilates with various esters, isotoicanhydride and anthranilamide.In this paper, we report the synthesis and characterization of 4*H*-3,1-benzoxazin-4-one and quinazolin-4-imine compounds **(1-6)**. In addition, all the compounds were evaluated for their antioxidant activity using DPPH radical scavenging.

EXPERIMENTAL

Thin layer chromatography (TLC) analysis was conducted by using thin aluminium plate of Merck Silica gel 60F254 of 0.2 mm thickness. The spots on TLC were visualized using Ultraviolet at 254nm and 365nm. The purification of compound was carried out by column chromatography using Merck Silica gel and the eluent used was mixture of hexane acetone in the ratio of 40:60. The products were characterized by using ATR and ^{1}H NMR. Sample product was measured on Attenuated Total Reflectance (ATR) with 20 scans for each sample at a resolution of 4cm^{-1} per measure. The IR spectra was recorded on PerkinElmer FT-IR Spectrometer Frontier. The ^{1}H spectra were obtained using 300MHz spectrometer for benzoxazinone and 400MHz spectrometer for