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Synthesis of Xanthone From 2-Phenoxybenzoic Acid Using Sulfuric Acid Catalyst

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Abstract: ***Synthesis of xanthone was extracted from 2-phenoxybenzoic acid by means of acid catalyzed cyclization. The products were characterized using FT-IR, ^{1}H-NMR, ^{13}C-NMR, LC-MS, spectrometers. Cyclization of 2-phenoxybenzoic acid using sulfuric acid catalyst resulted xanthone in 94.0% productivity.***

Keywords: xanthone, 2-phenoxybenzoic acid.

1. Introduction

Indonesia is well known as a rich country in natural resources, such as plants, minerals, and other substances. From generation to generation, many of them, especially the tropical plants, are utilized as traditional medicines to maintain the health quality, to prevent as well as to cure diseases. However, lots of their applications in the medical aspect have not been based on the scientific studies. To make the traditional medicine more applicable and useful in the formal or legal health services, sufficient research which is scientifically reliable is required to carry out.

One of the tropical plants used as the traditional medicine is the plant *Garcinia dulcis*. It is classified as the family of *Gutterferae* and can be easily found in Indonesia (well known as mangosteen plant). This plant has been proven to exhibit antiplasmodial activity. Ethanol fraction from the root of *G. dulcis* exhibit antiplasmodial of 15.21 µg/mL **[1], [11], [12].** From 400 *Garcinia* plants, it was found that xanthone was the major component, beside terpenoid, benzophenone and biflavonoid. Xanthone (Figure 1) has been known to exhibit potential biological activies. Xanthone and its derivatives are mainly existed on the fruit, leaves, bark and the root of *G. dulcis* tree. Research on xanthone isolated from the root of *G. dulcis* has been reported by Amanatie **[2]**. The application of xanthone as anti plasmodium agent, however, has not been much reported yet.

Figure 1: Structure of xanthone

This research was firstly conducted by extracting and identifying the xanthone from *G. dulcis* **[2]–[3]**. However, the result was very low, thus, the researcher tried to get the xanthone in higher amount via the synthesis process. The specific problems being formulated were:

1. How to optimally synthesize xanthone from 2-phenoxy benzoic acid?
2. How effective is the synthesis of xanthone?

This research was conducted with the main aims of synthesizing the xanthone. The specific objectives were:

1. To synthesize xanthone from of 2-phenoxybenzoic acid;
2. To analyze the synthesized xanthone derivatives using spectroscopy method (FTIR, ^{1}H-NMR, ^{13}C-NMR, and LC-MS spectrometer).

Xanthone and its derivatives were commonly obtained from the isolation of natural products. Isolation of xanthone has been conducted from the leaves **[4]** and bark **[5]** of *Garcinia dulcis*. Likhitwitayawuid **[6]-[7]**has obtained new xanthone derivatives of 7-O-methyl garci-non-E from *G. cowa* with IC_{50} of 1.50-3.00 µg/mL. Other xanthone derivatives of 1,3,7-trioxygenated and prenylatedxanthone have been isolated from Calophylum caledonicum **[8]**, **[13]** In addition **[2]** has reported that the IC_{50} of the root extract of *G. dulcis* was 15.21 µg/mL. The synthesis of xanthone from 2-phenoxybenzoic acid has also been conducted.

2. Theoretical Background

Identification of xanthone

Chemically, xanthone is different from flavonoid as can be seen in the characteristic spectra **[9]**. Xanthone could be isolated using a thin layer chromatography (TLC) with solvents of chloroform:acetic acid (4:1) chloro-form:benzene (7:3) or chloroform:ethyl acetate in various ratios. It could produce color given the reaction with ammonia under the UV light. Mangiferin (Figure 2) is practically different from all xanthone as it is soluble in water and can be well separated using paper chromato-graphy. Xanthone has the maximum wave lenghts in the range of 230-245, 250-265, 305-330 nm. Like flavonoid, xanthone gives the characteristic of bathochromic shift by the reaction with base, aluminum chloride, and sodium acetate-boric acid **[9].**

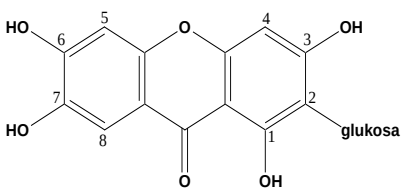

Figure 2: Structure of Mangiferin

Synthesis of xanthone

Xanthone could be synthesis from 2-phenoxybenzoic acid via cyclization reaction using sulfuric acid catalyst **[3] and [10]**. The reaction is displayed in Figure 3.

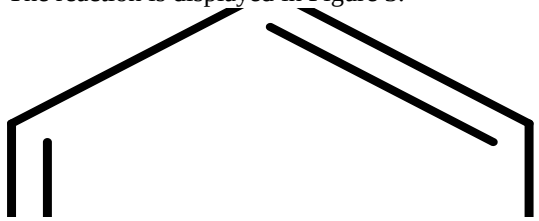

Figure 3: Synthesis of xanthone from 2-phenoxybenzoic acid

3. Method

3.1 Materials

For the synthesis, extraction, TLC, column chromatography and crystallization processes, the materials used were, 2-phenoxybenzoic acid, sulfuric acid, sodium hydroxide, sodium sulfat anhydrous, and aquadest. All the chemicals except aquadest were purchased from Merck.

3.2 Tools

For the synthesis, separation and purification purposes, several tools were used. There were laboratory glassware, vacuum pump, electric heater, magnetic stirrer, TLC apparatus, UV lamp, rotary evaporator and column chromatography apparatus. Characterization of the product was conducted using melting point apparatus (electrothermal 9100), infrared spectrometer (FTIR 8201 Shimadzu PC), proton nuclei magnetic resonance (^{1}HNMR JOEL, JNM MYGO 60 MHz, ^{1}HNMR JOEL, JNM ECA 500 MHz) and liquid chromatography-mass spectrometer (LC-MS Shimadzu GC-17 A QP-500.).

4. Result and Discussion

4.1 Synthesis of xanthone

Xanthone was synthesized via acid-catalicized-cyclization of 2-phenoxybenzoic acid **[10]**. The product was obtained as yellowish white needle crystal with m.p. of 173.5-173.9°C (theoretical m.p. of 172-174 $^{\circ}$C) in 94.0% yield. Elucidation of the product was conducted using UV-VIS, FT-IR, NMR and LC-MS spectrometers.

The UV-Vis spectrum gave 4 maximum wave-length at 334, 258, 236 and 202 nm. Furthermore, FT-IR spectrum showed strong absorption at 1689 cm^{-1} indicating the presence of carbonyl group (C=O). Peaks at 1604-2962 cm^{-1} showed functional groups of C=C and aromatic C-H. Band in the region of 1095-1141 cm^{-1} indicated the aromatic ether. According to IR spectrum, it could indicate that the synthesized product contained carbonyl, aromatic and ether groups.

^{1}H-NMR spectrum showed 4 peaks depicting 4 protons with different chemical environment. All peaks appeared in the absorption region of benzene ring. Peak of $H_1$and H_8 appeared at δ_H=8.3 ppm (*d*, *J*=7.65). Peak of H_2 andH_7existed at $\delta_{H=}$7.8 ppm (*t*, *J*=7.65). Protons of H_4 and H_5 gave peaks at δ_H=7.6 ppm (*d*, *J*=8.4). Then, protons of H_3 and H_6 gave peaks at δ_H=7.4 ppm (*t*, *J*=7.6).

^{13}C-NMR spectrum showed 7 carbon peaks. Peak at δC 179 ppm showed the presence of C_{13} of carbonyl group. Absorption at δC 122 ppm came from C_9 and C_{12}. Carbon of C_1 and C_8 gave peaks at δC 127 ppm. Carbon of C_2 and C_7 gave peaks at δC 119 ppm. Carbon of C_3 and C_6 gave peaks at δC 125 ppm. Peak for C_4 and C_5 was at δC 136 ppm, while that for C_{10} and C_{11} was at δC 157 ppm.

Based on LC analysis, there was one peak at retention time of 46 minute. The peak was then analyzed using MS to find the molecular weight of compound. Method of MS applied in this analysis was ESI-MS positive ion. The spectrum of ESI-MS showed several peaks. The peak b with m/z 197.23 was the base peak. It represented the protonated product $[M + H]^+$ ion. Therefore the molecular weight of the product was 196, i.e. the molecular weight of xanthone.

According to UV-Vis, IR, ^{1}H- and ^{13}C-NMR as well as LC-MS analyses, it could be concluded that the product was xanthone (Figure 4) with the molecular formula of $C_{13}H_8O_2$.

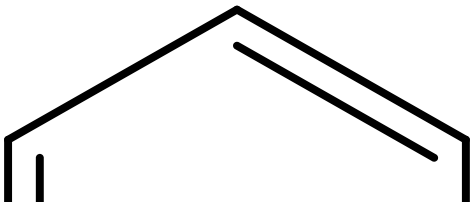

Figure 4: Synthesis of xanthone from 2-phenoxybenzoic acid

5. Conclusion and Suggestion

5.1 Conclusions

According to results and discussion, it could be concluded that: Acid-catalyzed cyclization of 2-phenoxybenzoic acid produced xanthone in 94.0% efficiency.

5.2 Suggestion

According to results and discussion previously explained, it can be suggested that the reaction conditions in the synthesis of xanthone should be optimized to get the higher result.

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Author Profile

Amanatie received her B.S. degree in Chemistry Education from IKIP Yogyakarta (1979), M.Ed degree in Educational Research and Evaluation from IKIP Jakarta (1996), M.S. and Ph.D. degrees in Chemistry from Gadjah Mada University (2000 and 2013, respectively). She has started her research as antimalarial agents since 2004, and is now focusing on Xanthone derivatives from 2-phenoxy benzoic acid. She teaches at Yogyakarta State University.