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RESEARCH PAPER

Synthesis and characterization of 2,4,6-trihydroxy benzophenone and its activity as sunscreen

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Abstract: Benzophenone was synthesized through a condensation reaction of benzoic acid and phloroglucinol with an Eaton reagent as a catalyst. The percentage of the product was 60%, and it was characterized using FTIR and 1H-NMR. The sunscreen activity was carried out using a UV-Vis spectrophotometer to calculate the SPF value. The synthesis result was made in several concentration variations: 100, 150, 200, 250, and 300 ppm to measure the SPF values. The results showed that the SPF values were 9.89, 13.39, 17.83, 23.77, and 28.26, respectively. Based on this, it can be concluded that these compounds have biological activity as sunscreen and samples of 200-300 ppm are included in the ultra-category as sunscreen.

Keywords: Sunscreen, 2,4,6-Trihidroxy benzophenone, and SPF

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INTRODUCTION

Benzophenone is a precursor compound widely used as an active ingredient in cosmetics and medicine. It has an important function, especially protecting skin from UV radiation (UV filter). Many commercial benzophenone derivatives are used as UV-filter, including benzophenone (BP), 2,2',4,4'-tetrahydroxybenzophenone (BP-2), 2,4-dihydroxybenzophenone (BP-1), 2,2'-dihydroxy-4-methoxybenzophenone (BP-8), 2-hydroxy-4-methoxybenzophenone (BP-3), 5-benzoyl- 4-hydroxy-2-methoxybenzenesulfonic acid (BP-4) [1-7], but the use of commercial benzophenone has started to worry due to its high accumulation in the environment, especially BP-3 and BP-4 [8,9].

Another benzophenone widely used is 2,3,4-trihydroxybenzophenone (2,3,4-OH-BP, THB). Trihydroxy benzophenone (THB) is an alternative compound due to its low toxicity and rarely detected in the environment. The presence of trihydroxy benzophenone is another alternative to reduce the toxicity of other dihydroxy benzophenone derivatives. Nowadays, the synthesis of benzophenone also can be obtained through the oxidation of diphenylmethane using nano Co-Mn catalyst, oxidation with nitric acid [11,12], chromic acid [13,14], and potassium permanganate [15,16], Fries rearrangement from diaryl ester derivatives [17-20], cycloaddition of diels alder [21-25], one-pot reaction of benzene in the $CCl_4 \cdot AlCl_3$ complex system [26-30]; aerial-oxidative benzanullation reaction [31-32]. Another more selective and optimal strategy for obtaining benzophenone is synthesis through the xanthone synthesis pathway, which also produces high yields, namely the Friedel-Craft acylation pathway between benzoyl chloride and benzene derivatives [33-36]. Synthesis of another THB compound analogue in the form of 2,4,6-trihydroxybenzophenone through a one-pot reaction was continued by testing its activity as sunscreen using UV-Vis spectrophotometer by measuring the value of the Sun Protecting Factor (SPF).

MATERIALS AND METHODS

Synthesis of 2,4,6-Trihydroxy Benzophenone

The synthesis was carried out through benzoic acid and phloroglucinol (1:1) reaction with Eaton reagent as a catalyst. Each material was put into a three-neck flask and heated at (80 ± 3) °C for 3 hours. Then, the mixture was allowed for 1 hour to reach room temperature. After that, it is poured into ice water and stirred for 1 hour until a precipitate is formed. The precipitate was filtered by vacuum filtration and dried for ± 24 hours in a desiccator. The product was characterized by FTIR and ^{1}H-NMR.

Sunscreen Activity Test

The sample was dissolved in pure ethanol to prepare a 1000 ppm solution. This solution was diluted to obtain various 100, 150, 200, 250 and 300 ppm concentrations. The absorbance of each solution that had been prepared and pure ethanol was measured by UV-Vis spectrophotometer at 290-320 nm wavelength with an increase of 5 nm.

RESULTS AND DISCUSSION

Synthesis of 2,4,6-Trihydroxy Benzophenone

The mechanism of 2,4,6-trihydroxy benzophenone synthesis begins with protonation on the carbonyl group of benzoic acid by methane sulfonate. The protonation occurs immediately in the reaction due to methane sulfonate acting as a protonation agent (electrophile). At the same time, methane sulfonate was also an acylation agent.

The next reaction was condensation between the carbocation of benzoic acid and phloroglucinol, forming an intermediate benzophenone compound. Phloroglucinol, in this case, acts as a nucleophile that attacks the carbocation. The nucleophilic of phloroglucinol was very strong because it has 3 hydroxy groups, which can activate the aromatic ring of phloroglucinol in the ortho and para positions (electron-donating substituents).

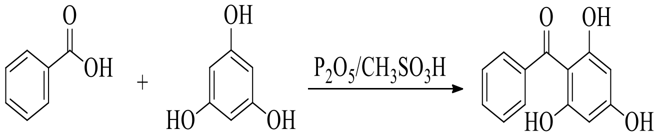

Figure 1. Synthesis pathway of 2,4,6-trihydoxy benzophenone

The intermediate compound formed is unstable; this is due to the influence of the methane sulfonate group, which is still bound to the carbon atom. The methane sulfonate group has a high electron density, which causes the electrophilic of the carbon atom to increase to gain stability; the methane sulfonate group is released through the deprotonation and diacylation reaction.

The product was characterized using FTIR, which shows a typical absorption peak at 3459 cm^{-1}, 1609 cm^{-1}, 1487 cm^{-1}, and 3141 cm^{-1} wave number. The absorption peak at 3459 cm^{-1} shows the hydroxy group bound in terms of the shape of the absorption peak, which tends to be sharp. It is probably due to the influence of the aromatic bonds formed in the reaction.

The absorption peak at 1609 cm^{-1} indicates the chelated carbonyl group, which is supported by the appearance of hydroxy groups, while the absorption peak at 1487 cm^{-1} indicates a typical absorption of aromatic ring bonds (C=C), then 3141 cm^{-1} 1 shows the stretching of C-H groups. This research was supported by a previous study that there was an absorption peak of chelated carbonyl at 1639 cm^{-1}, the hydroxy group bound at 3383 cm^{-1}, and the absorption of aromatic groups at 1512 cm^{-1} [37].

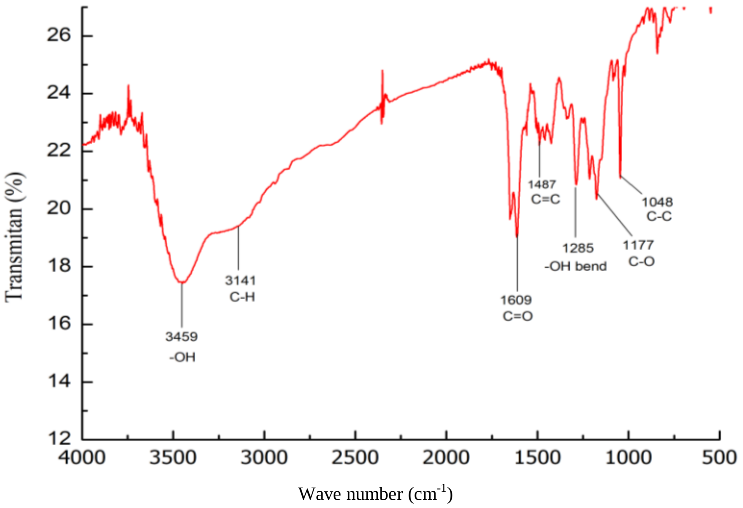

Figure 2. Result of FTIR characterization

Based on the ^{1}H-NMR spectrum, a proton signal appears at a chemical shift of 8.22 ppm (d, 1H), indicating hydroxy chelate proton's presence at the C-2 position. The appearance of the hydroxy proton signal in the deshielding area (unshielded) is due to the influence of the inductive effect of the oxygen atom on the hydroxy and oxygen of the carbonyl group. The induction effect shifts the protons into the weak field; therefore, the signal appears in the deshielding area.

The proton signal also appears in a range of 6-8 ppm for aromatic. 5 proton signals appear in the aromatic region, 4 from aromatic protons, while 1 signal is a signal from another hydroxy proton. Based on the data, the proton signal at a chemical shift of 7.83 ppm (2H, J=7.2 Hz) was a proton signal at C-2' and C-6' positions. It is because the protons of C-2' and C-6' are the most deshielding protons compared to other aromatic protons, then followed by protons with a weak field level, respectively, at positions C-4', C-3' and C-5', C-3 and C-5.

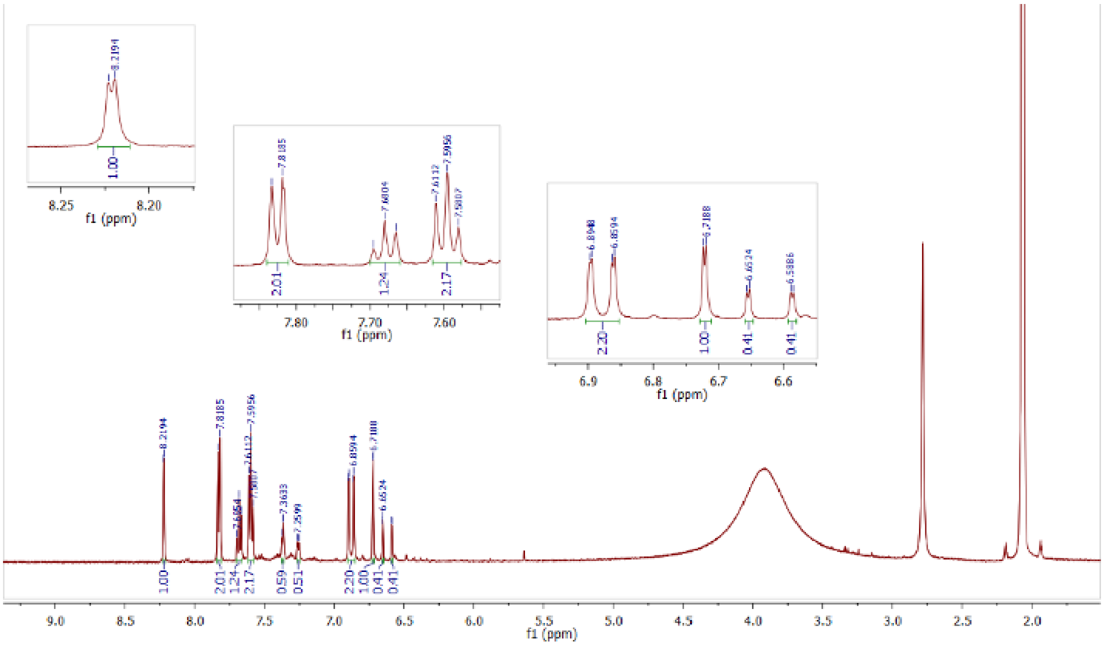

Figure 3. Result of H-NMR characterization

The position of the protons is also amplified by the coupling constant, which indicates the environment of the protons. Proton signal at C-2' and C-6' positions show a coupling constant of 7.2 Hz, which indicates ortho correlation with protons at C-3' and C-5' positions (J=7.6 Hz). Ortho correlation also occurs between protons in C-3' and C-5' positions with protons in C-4' positions (J=7.5 Hz). The protons of the hydroxy group at C-2 and C-6 positions have meta-correlation as indicated by the coupling constant values of 1.8 Hz and 2.2 Hz, respectively.

Sunscreen Activity Test with UV-Vis Spectrophotometer

Based on the results of measurements using a UV-Vis spectrophotometer, the absorbance values were obtained at 290-320 nm wavelength. This absorbance value calculates the SPF (Sun Protecting Factor) value of the synthesized compound with various concentrations of 100, 150, 200, 250 and 300 ppm. The calculation of the SPF value using the following equation:

$$\mathrm{SPF} = \mathrm{CF} + \sum_{290}^{320} \mathrm{EE}\ x\ \mathrm{I}\ x\ \mathrm{absorbance}$$

Information:
CF = Correlation Factor (10)
EE = Erythema Efficiency
I = Light intensity spectrum

Table 1. Data on SPF value of 2,4,6-trihydroxy benzophenone

Concentration (ppm)	SPF
100	9.89
150	13.39
200	17.58
250	23.77
300	28.26

Based on the calculation, the SPF value was obtained in the range of 9.89-28.26, which is the highest SPF value indicated by a sample of 300 ppm concentration (Table 1). Based on the SPF value obtained, it can be seen that the synthesized compound is active as a sunscreen. The increasing value of SPF indicates this, along with increasing sample concentration. This sunscreen activity is probably due to the 2,4,6-trihydroxy benzophenone compound, which is an organic compound that has an ortho- or para-substituted benzene nucleus conjugated with the carbonyl group [37] , is caused by the presence of a chromophore (π→π^ *) which absorbs in the UV light region, namely the double bond in benzene.

CONCLUSION

Based on the research, it can be concluded that the sunscreen activity of 2,4,6-trihydroxy benzophenone through condensation reaction between benzoic acid and phloroglucinol using eaton reagent catalyst showed the activity as sunscreen at various concentrations of 100, 150, 200, 250, and 300 ppm with a range of SPF value 9.89-28.26. Samples with 200-300 ppm concentration are classified as ultra sunscreen.

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