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Use of the compound (2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one) as a ligand complex formation by copper (II)

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ABSTRACT

Flavonol compounds are chalcone derivatives, generally found in hydroxy substituted forms that can act as ligands. Hydroxy-substituted flavonols are found in many plants but in very small amounts. In order to enrich and expand the use of this compound as a ligand, the synthetic methods were carried out through structural variations, one of which was by substitution using chloride and then the compound (2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one) was obtained. In this research, the study was conducted using the compound (2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one) as a ligand for complex formation with copper (II). From the results of the study, the mole ratio of the ligand with copper (II) metal was 2:1, pH 7.01 with a complex stability time of 15-25 minutes. The complex formed is bright yellow in color and soluble in chloroform. From the characterization of the resulted complex, it was appeared that Cu-flavonol chloride with UV-Vis spectrophotometer showed maximum absorption at wavelengths 273 and 429 indicating the presence of benzoyl and cinnamoyl peaks, with FT-IR showing the wave number 1545cm⁻¹ indicating the presence of Cu=O-Cu bonds and absorption at 682 cm⁻¹ indicating the presence of Cu-O bonds.

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1. Introduction

Flavonols are chalcone-derived compounds known as secondary metabolites and belong to the flavonoid class. In plants, these compounds are generally found in a hydroxy-substituted form, although in very small amounts. The presence of free electrons from the 5-hydroxy and 4-ketone functional groups substituted in the flavonol structure plays a very important role in bioactivity, such as antibacterial and cardiovascular effects and can act as ligands in the formation of complex compounds with metals.^{1,2} Several studies have reported the synthesizing of complex compounds from several hydroxy substituted flavonol compounds with metals such as metal ions Cr, Tb, Rh, Mg, Zn and Fe.³⁻⁶ To enrich and expand the use of this compound as a ligand, synthesis was carried out through structural variations, one of which was by substitution using chloride. The presence of chloride is expected to affect the induction effect so that there is a shift in the electron density of the functional group and the level of stability of the complex.⁷⁻⁸

Structural variations with chloride substitution have been successfully carried out through the Flynn-Algar-Oyamada (FAO) reaction of the compound 2'-hydroxychalcone,(E)-3-(4-chlorophenyl)-1-(2-hydroxyphenyl)prop-2-en- 1-0n with H₂O₂ in an alkaline solution produced a new compound in the form of a chloride substituted flavonol, namely the compound (2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one).^{9,10} From a preliminary test using flavonol-chloride as a ligand for several central ions, the complex with Cu(II) showed a distinctive color change compared to using other transition metals.¹¹ According to Suciningrum, copper as the central atom has the greatest complex ion stability compared to other fourth period transition metals.¹² As research by Ríha et al. has synthesized metal complex compounds Cu(II) with 3-hydroxyflavone ligands showed that flavonols as bidentate ligands were formed with a stoichiometric ratio of 2:1 in the pH range 5.5 – 7.5.¹³

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Heterocyclic compounds constitute the largest diversity of organic molecules of chemical, biomedical, and industrial significance.¹⁴⁻²¹ For the formation of Cu complexes with flavonol chlorides, it is necessary to know the mole ratio of ligands and metal ions, complex stability time and optimal environmental pH. pH plays an important role in complex formation because, in high acidity environmental conditions there will be a decrease in the ability of the ligands to interact with metal ions, because the ligand is difficult to deprotonize. On the other hand, in an alkaline environment there will be a lot of hydroxy ions which will deprotonate the ligand so that the complex is easier to form and more stable

2. Research Methods

2.1. Materials

The tools used in this study were a microwave (Samsung ME109F), UV-Vis spectrophotometer (Agilent Technologies, Cary 60), FT-IR spectrophotometer (Shimadzu, IR Prestige-21), HPLC (Shimadzu LC Solution column type Shim-pack VP-ODS with length and diameter of 150 x 4.6 mm), GF254 silica TLC plate, UV lamp (254 and 366 nm), vacuum pump (ABM type 4EK F6 3CX-4) and synthesis equipment commonly used in laboratories. The materials used in this study were 2-hydroxy acetophenone, 4-chlorobenzaldehyde, copper(II) sulfate pentahydrate, KOH, HCl, 30% H₂O₂, aqua DM, and various organic solvents.

2.2. Synthesis of compounds (2-(4-chloro phenyl)-3-hydroxy-4H-chromen-4-one)

A total of 0.5 mmol of 2'-hydroxychalcone compound was dissolved in 5 mL of ethanol and 1 mL of 3N KOH was added. The mixture was cooled to 10°C. Then add 0.25 mL of 30% H₂O₂ to the mixture and irradiated with a microwave at 180W for 2 minutes. Every 30 seconds the reaction was tested by TLC. After the reaction was complete, 5 mL of 10% cold HCl was added dropwise to the mixture until a precipitate was formed. The precipitate was filtered using Whatman 42 filter paper. Then it was washed with cold distilled water and n-hexane. The solids were dried to obtain pure chloride substituted flavonols tested based on TLC analysis, melting point and HPLC.

2.3. Synthesis of Cu(II)-(2-(4-chlorophenyl)-3-hydroxy-4-chromene-4-one complexes)

A total of 10 mL (1 mmol) of compound (2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one) in ethanol solvent was added to Erlenmeyer. Then slowly add 10 ml of copper sulfate pentahydrate solution (0.5 mmol) and stir for 1.5 hours at room temperature, the precipitate formed is filtered using filter paper with the help of a vacuum pipe. The precipitate of complex compounds on filter paper was washed with ethanol solvent: water (3:1).

2.4. Determination of the optimum pH for the synthesis of copper (II)-flavonol chloride complex compounds

A total of 10 mL of 2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one with a concentration of 10⁻³ M was put into an erlenmeyer. Slowly add 5 mL of 10⁻³ M solution of copper (II) sulfate pentahydrate at pH 4.03 and add 5 mL of chloroform, stirring the solution using a magnetic stirrer at 300 rpm for 20 minutes at room temperature. The chloroform solvent was separated from the mixture using a separating funnel and collected into a vial. Then the solution was placed in a cleaned cuvette and its absorbance was measured with a UV-Vis spectrophotometer using a wavelength of 429 nm against a chloroform blank. Do the same for variations in pH 5.00; 6.01; 7.01 and 8.08).

2.5. Determination of stability time of copper(II)-flavonol chloride complex

A total of 10 mL of 2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one with a concentration of 10⁻³ M was put into an erlenmeyer. Slowly add 5 mL of 10⁻³ M copper (II) sulfate pentahydrate solution at optimal pH and add 5 mL of chloroform, stirring the solution using a magnetic stirrer at 300 rpm for 20 minutes at room temperature. The chloroform solvent was separated from the mixture using a separating funnel and collected into a vial. Then the solution was placed in a cleaned cuvette and its absorbance was measured with a UV-Vis spectrophotometer using a wavelength of 429 nm every 5 minutes for 2 hours.

3. Results

3.1. Synthesis of compound (2-(4-chlorophenyl)-3-hydroxy-4H-chromen-4-one)

The formation of the compound (2-(4-chloro phenyl)-3-hydroxy-4H-chromen-4-one), begins with the elimination of hydrogen at the carbon α position of the 2'-hydroxyacetophenone compound in an alkaline solution. The elimination of hydrogen at this position occurs due to the absorption of OH⁻ ions from the base which acts as a nucleophile to form phenoxide ions.⁹ The reaction for the formation of chloride substituted flavonols can be seen in **Fig. 1**. The purity of the compound (2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one) was proven by TLC test where R_f = 0.54 while R_f of 2'-hydroxychalcone = 0.86. This shows that flavonol chloride compounds have been formed which have greater polarity than

2'-hydroxychalcone compounds. Melting point test obtained temperature intervals that are less than two, namely between 157 – 159°C. The functional group test with FT-IR obtained several types of vibrations, including C-Cl at wave number 760cm^{-1} , C-O at 1108cm^{-1} , C=C at 1560cm^{-1} , aromatic C-H at 3109cm^{-1} and O-H at 3284cm^{-1} . Meanwhile, the characterization using UV-Vis spectrophotometry showed that there were 2 maximum peaks, namely the benzoyl and cinnamyl peaks contained in the structure of the compound at a wavelength of 243nm, 344nm (Figure 2). Ensafi et al., said that flavonol group compounds will give 2 maximum peaks in their electronic spectrum caused by the electron transition ($\pi - \pi^*$).²²

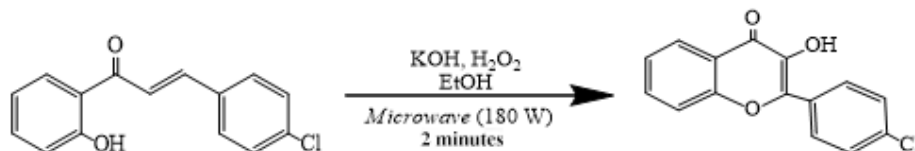


Fig. 1. Reaction for formation of chloride-substituted flavonols

3.2. Synthesis of Cu(II) - (2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one Complex)

The formation of complex compounds with flavonol ligands occurs when the occupied orbitals of the flavonol ligands hybridize (overlap) to the empty copper (II) metal ion orbitals to form sp^3d^2 hybridization. Based on the valence bond theory, the sp^3d^2 hybridization of the complex formed is an outer sp^3d^2 orbital so that it is possible that the complex formed is relatively unstable. Copper(II) metal can form a d^9 system complex with a distorted octahedral geometry due to the Jahn Teller stabilization energy. This distorted octahedral geometry is more stable than the copper(II) complex tetrahedral geometry. This distorted geometric shape also results in only 2 substituted flavonol ligands (bidentate ligands) because there are 2 lone electron pair donor sites, namely the 4 keto and 3 hydroxy sites. The hydroxy site is a stronger nucleophile than the chloride substituted at the para position.^{23,24} This causes the formation of complex compounds to be more likely to occur in the hydroxyl group than chloride, so that it is more difficult for chloride to donate its electron pair, meaning that the substitution of chloride does not specifically affect the formation of complexes with the central Cu(II) atom.

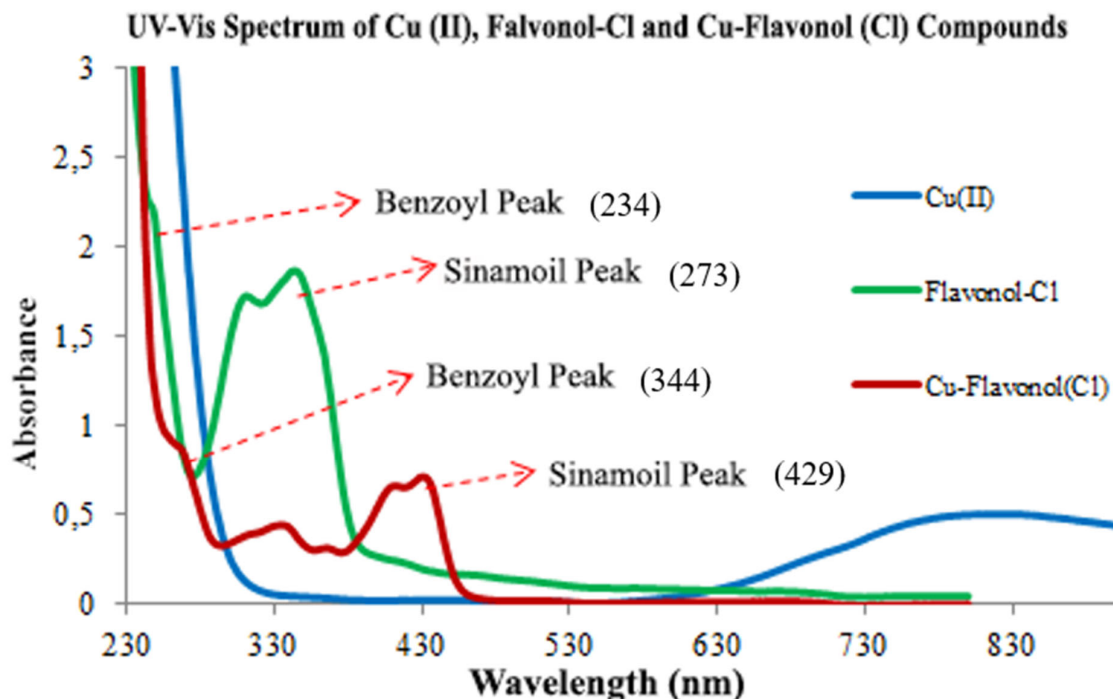


Fig. 2. Peak shift in the benzoyl system and sinamoil

3.3. Complex characterization of Cu(II)-(2-(4-chlorophenyl)-3-hydroxy-4H-chromene-4-one)

Based on solubility, Cu-flavonoid chloride complex is slightly polar and more soluble in cloform. From the FT-IR spectra of complex compounds, the coordination covalent bonds of complex compounds between C=O in flavonols and Cu metal (C=O-Cu bonds) appear indicated by the appearance of an absorption band of 1545cm^{-1} . The formation of this

coordination bond causes the vibration of the C=O bond in the organic molecule. The absorption band of the C=O group in the complex changed to a wave number of 1605cm^{-1} . In addition, the formation of Cu-O bonds was indicated by the appearance of absorption at a wave number of 680cm^{-1} , besides that the formation of complexes was also indicated by the occurrence of a bathochromic red shift of the cinnamoyl system from 346nm to 429nm . This is in accordance with the results of research Souza et al. have synthesized a complex of Cu with 3-hydroxyflavones to produce a spectrum, FT-IR at 610cm^{-1} band and a bathochromic shift of the cinnamoyl peak at 343nm to 359nm . The FT-IR spectrum is shown in Fig. 3.²⁵

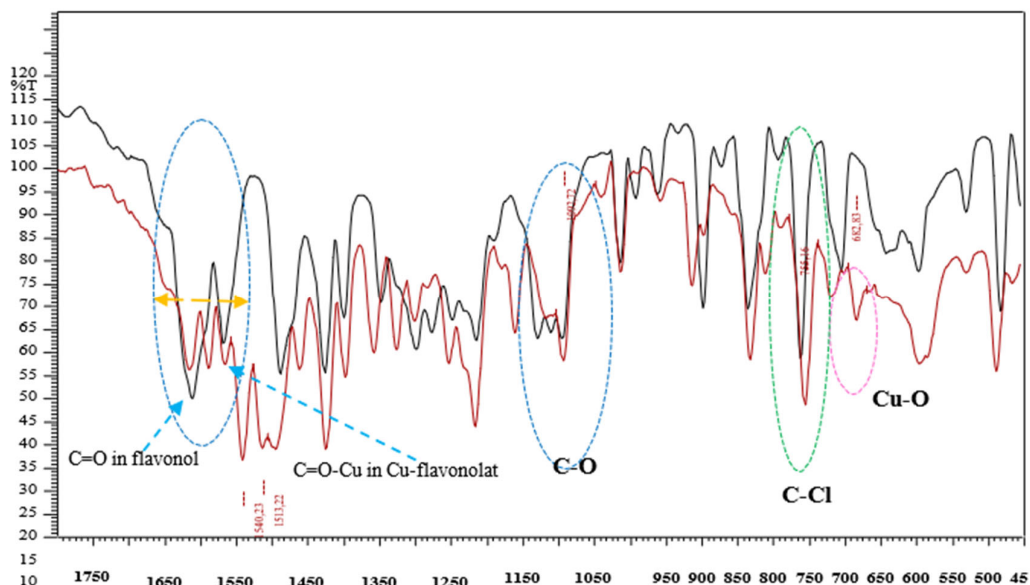


Fig. 3. FT-IR spectrum of flavonol chloride and Cu(II) flavonol chloride compounds at wave numbers $1750\text{--}450\text{ cm}^{-1}$

3.4. Determination of the optimum pH of the Cu(II)-flanonol chloride complex

In general, Cu(II) complex formation reactions can occur in the pH range of 4 – 7. Říha et al., synthesized 3-hydroxyflavones to form complex compounds with Cu(II) metal showing flavonols as bidentate ligands with a stoichiometric ratio of 2:1 in the pH range of 5.5 – 7.5.¹³ From the research results, it can be seen that the optimal pH is reached at pH 7.01. Under acidic conditions (pH 4 and 5) a shift in equilibrium occurs due to protonated flavonols so that the equilibrium shifts towards the reactants. Protonation of flavonol compounds will reduce its ability as a ligand to donate electron pairs. This is because protonation of the carbonyl group will form a positive synthone (lack of electrons) which will tend to like nucleophiles and there is a steric hindrance. The steric hindrance at this site makes it difficult for copper (II) metal to interact with its electron pair donor group. It is also possible that there is complex formation at the chloride B ring site. However, the complex at the chloride site has a lower level of stability. The low stability is due to the presence of chloride with a higher electronegativity than oxygen so that the distribution of electrons in metallic bonds with ligands is uneven. Under alkaline conditions (pH 8), $\text{Cu}(\text{OH})_2$ tends to form, causing the reaction equilibrium of complex compounds to shift towards the reactants (Fig. 4).

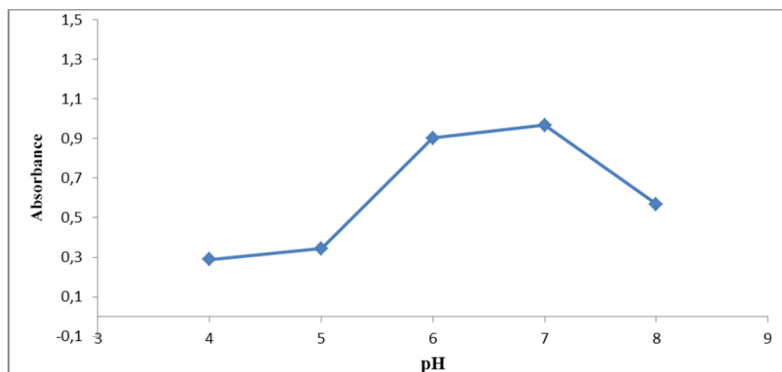


Fig. 4. The results of the measurement of the absorbance of the synthesis of complex compounds in various pHs with a synthesis ratio of 2:1

4. Conclusion

Based on the results of the research, it can be concluded that the synthesis of the Cu(II)-flavonol chloride complex showed an optimal mole ratio of 2:1 with a stability period of 25-35 minutes at pH 7.01 (neutral). The Cu(II) flavonoid chloride complex is yellow in color and is well soluble in chloroform. The results of the characterization of the Cu(II)-flavonol chloride complex showed the presence of Cu-O bonds at 682 cm^{-1} and C=O-Cu bonds) absorption band at 1545 cm^{-1} .

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