Kelubi Fruit (*Eleiodoxa conferta*) extract as a Green Catalyst Synthesis of 3,4-dihydropyrimidin-2 (1H)-ones

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**Abstract.** The use of synthetic strong acid catalysts or lewis acid catalysts from metals often causes environmental problems at the end of a chemical reaction. In this research offers an alternative solution using kelubi fruit extract (*Eleiodoxa conferta*) as a green catalyst, especially in the synthesis of 3,4-dihydropyrimidin-2 (1H)-ones derivatives which are reported to be active as therapeutic and bioorganic chemistry. So the purpose of this research was to develop a green catalyst from natural fruit for the synthesis of 3,4-dihydropyrimidin-2 (1H)-ones using kelubi fruit. The Green catalysts are obtained from water extracts of kelubi fruit that are ripe. Then the catalyst is added to the reagent for the synthesis of pyrimidine derivatives that consist of urea, benzaldehyde, and ethyl acetoacetate (equivalent). As a comparison, HCl is used as an acid catalyst. The result is the highest yield (67.7%) at the use of 0.2 ml green catalyst and reaction time 180 minutes. Spectrum UV-Vis of characteristics compound has a maximum wavelength of 306 nm.

1. **Introduction**

The need for therapeutic materials is still a priority for several aspects such as food, medical, and others. Compounds of 3,4-dihydropyrimidin-2 (1H) -ones exhibit activity as antiviral, antihypertensive, antimicrobial, anti-inflammatory [1]. Synthesis of compounds 3,4-dihydropyrimidin-2- (1H) -on from ethyl acetoacetic or methyl acetoacetic, urea or thiourea, and aromatic aldehyde substrate can use Lewis acid or Bronsted acid catalysts such as BF3:OEt2/CuCl, 12-molybdochosphoric acid [2], lanthanum nitrate [3], Bronsted Acid Ionic Liquid [4], benzyltrethylammonium chloride [5], p-dodecylbenzenesulfonic acid [6], trichloroacetic acid [7], titanium dioxide [8], acidic choline [9], Iron (III) tosylate [10], 1-glycyl-3-methyl imidazolium chloride-copper (II) [11], and Bis [(L) prolinate-N,O ] Zn–water [12]. The use of these catalysts has promising results with high yields and various times. But the drawback is the use of synthetic strong acid catalysts or Lewis acid catalysts from metals often causes environmental problems at the end of a chemical reaction. In addition, the use of catalyst reagents above is somewhat hazardous substances and expensive. So, this research offers an alternative solution using kelubi fruit extract (*Eleiodoxa conferta*) as a green catalyst, especially in the synthesis of 3,4-dihydropyrimidin-2 (1H)-ones derivatives which are reported to be active as therapeutic and bioorganic chemistry.

Kelubi fruit extract (*Eleiodoxa conferta*) or asam paya live in Southeast Asian countries, one of which is in Indonesia. Kelubi fruit (Eleiodoxa conferta) has been reported to contain 82.2% water, 0.8% protein, 3.1% fat, 11.8% carbohydrate, 11.8% fiber, and ash content 0.7%. In addition, the fruit also contains 18.3 mg of vitamin A, 1.1 mg of vitamin B1, 1.9 mg of vitamin B2, 1.6 mg of vitamin C, 11.8 mg of vitamin E, and 1.4 mg of phosphorus. Kelubi fruit is rich in fiber and ash, 11.8% of weight (Table 1).

Table 1. Composition of Kelubi fruit as a percentage of weight.

| Component       | Percentage |
|-----------------|------------|
| Protein         | 3.1%       |
| Fat             | 0.8%       |
| Carbohydrate    | 11.8%      |
| Fiber           | 11.8%      |
| Ash             | 0.7%       |
| Vitamin A       | 18.3 mg    |
| Vitamin B1      | 1.1 mg     |
| Vitamin B2      | 1.9 mg     |
| Vitamin C       | 1.6 mg     |
| Vitamin E       | 11.8 mg    |
| Phosphorus      | 1.4 mg     |

The fruit also contains 0.8% of water, 18.3 mg of vitamin A, 1.1 mg of vitamin B1, 1.9 mg of vitamin B2, 1.6 mg of vitamin C, 11.8 mg of vitamin E, and 1.4 mg of phosphorus. Kelubi fruit is rich in fiber and ash, 11.8% of weight (Table 1).

Kelubi fruit is rich in mineral elements such as calcium, iron, phosphorus, magnesium, potassium, and sulfur as shown in Table 2. Calcium is found in the form of CaCO3 in the form of calcite, aragonite, and dolomite. Iron is contained in the form of FeS, Fe3O4, and Fe2O3. Phosphorus is found in the form of P2O5, PO4, and H3PO4. Magnesium is found in the form of MgO and MgCO3. Potassium is found in the form of K2O and KCl. Sulfur is found in the form of SO2, SO3, and H2SO4. Kelubi fruit is rich in vitamin A, vitamin C, vitamin E, vitamin B1, and vitamin B2. Kelubi fruit (Eleiodoxa conferta) is reported to contain 82.2% water, 0.8% protein, 3.1% fat, 11.8% carbohydrate, 11.8% fiber, and ash content 0.7%. In addition, the fruit also contains 18.3 mg of vitamin A, 1.1 mg of vitamin B1, 1.9 mg of vitamin B2, 1.6 mg of vitamin C, 11.8 mg of vitamin E, and 1.4 mg of phosphorus. Kelubi fruit is rich in fiber and ash, 11.8% of weight (Table 1).

Table 2. Mineral element in Kelubi fruit as a percentage of weight.

| Mineral Element | Percentage |
|-----------------|------------|
| Calcium         | 11.0%      |
| Iron            | 1.7%       |
| Phosphorus      | 1.2%       |
| Magnesium       | 0.9%       |
| Potassium       | 1.1%       |
| Sulfur          | 0.8%       |
| Vitamin A       | 18.3 mg    |
| Vitamin C       | 1.6 mg     |
| Vitamin E       | 11.8 mg    |
| Vitamin B1      | 1.1 mg     |
| Vitamin B2      | 1.9 mg     |

The fruit also contains 0.8% of water, 18.3 mg of vitamin A, 1.1 mg of vitamin B1, 1.9 mg of vitamin B2, 1.6 mg of vitamin C, 11.8 mg of vitamin E, and 1.4 mg of phosphorus. Kelubi fruit is rich in fiber and ash, 11.8% of weight (Table 1).
contains minerals and vitamins such as K 227 mg, Ca 26 mg, Mg 22 mg, P 10 mg, Fe 5.5 mg, Zn 8.9 ppm, Mn 5 ppm, Cu 2.9 ppm, and ascorbic acid 0.6 mg [13]. This fruit (Eleiodoxa conferta) is also reported to contain anthocyanin in ethanol extract and is used as a dye-sensitized solar cells (DSSCs) with an efficiency of 1.00% [14]. And this fruit is active as an antibacterial [15]. In addition, the Kelubi fruit from the Bangka Belitung region is widely used as a mouth ulcer drug, used by people as a sour taste in cooking because the kelubi fruit has a sour and runny taste [15]. The sour taste derived from vitamins and minerals is used as a green catalyst for synthesis 3,4-dihydropyrimidin-2-(1H)-on via Biginelli reaction.

Several fruit juices that have been utilized in this reaction. Some fruit juices that have been reported such as grape juice [16], lemon juice [17], pineapple juice [18], lime (Citrus aurantifolia) [19], amla juice [20] and Tamarindus indica juice [21]. The results of the use of this fruit catalyst are not too bad when compared with the use of Lewis acid catalyst which is toxic. So this research develops the fruit as a catalyst for the synthesis of 3,4-dihydropyrimidin-2- (1H) -on compounds via Beginelli synthesis which is eco friendly and environmentally friendly.

2. Research methods
2.1 Acid Catalyst Preparation of Kelubi Fruit Extract (Eleiodoxa conferta)
The sample of this research is Kelubi fruit taken from Pergem Village, Airgegas Subdistrict, South Bangka Regency. Furthermore, the fruit was divided into two parts then squeezed using a filter. The resulting fruit water was then filtered gradually with a clean cloth and filter paper to get clean water from the fruit solids. Kelubi fruit extract water was used as a natural catalyst [17].

2.2 Synthesis of 3,4-dihydropyrimidin-2-(1H)-on with Kelubi Fruit Extract (Eleiodoxa conferta)
Vanillin (2.12 g 20 mmol) (1), ethyl acetoacetate (2.6 g, 20 mmol) (3), Urea (1.2 g, 20 mmol) (2) and 0.5 ml of kelubi fruit acid catalyst were added to the Erlenmeyer, then distilled at a temperature 50 °C for 15-180 minutes. Stop the stirrer and warm-up, the reaction mixture has solidified and then added 8 mL of ethanol and heat at 50 °C for 10 minutes then filter the results. The filtrate is then placed in a refrigerator for 1 day until crystals are formed and then filtered to obtain filtrate and solids. Then recrystallization using ethanol. The resulting crystal was white colour and then filtered with filter paper of known weight. The crystals were dried in an oven at 100 °C. Finally, the calculation was done to find out the product yield. The crystals from the purification product (± 50 mg) were put into the watch glass then a little (0.1 - 0.5 mL) of chloroform was added until completely dissolved. The solution was then bottled on a TLC (Thin Layer Chromatography) plate. The TLC plate was then eluted using n-hexane : Ethyl acetate (6: 4) as an eluent. The product was analyzed using UV-Vis spectrophotometer 1800 Shimadzu, and FT-IR thermolyne spectrophotometer.

3. Result and Discussion
3.1 Acid Catalyst of Kelubi Fruit Extract (Eleiodoxa conferta)
The resulting Kelubi fruit extract was centrifuged and filtered until a red Kelubi fruit extract was produced as shown in Figure 1. The red color of the kelubi was caused by the presence of anthocyanin compounds as reported by Jaafar et.al. [14]. In acid conditions, anthocyanins are red [22]. The acidic nature of the fruit of the kelubi due to ascorbic acid and some minerals makes the anthocyanin in the Kelubi fruit to form a red flavylium cation. So that the nature of this natural acid is used as a green catalyst.

Figure 1. (a) The kelubi fruit, (b) the catalyst of the kelubi water extract
3.2 Synthesis Product of 3,4-dihydropyrimidine-2-(1H)-on

Synthesis of 3,4-dihydropyrimidine-2- (1H) -on in this study uses vanillin substrate. Generally, the substrate is used using benzaldehyde compounds. Vanillin itself is a derivative of benzaldehyde. The reaction results were monitored using TLC with n-hexane: ethyl acetate (6: 4) as the eluent. The chromatogram is presented in Figure 2. The Rf (retention factor) value of the product (3,4-dihydropyrimidine-2- (1H) -on) is lower than that of the substrate (vanillin). This shows that the compound 3,4-dihydropyrimidine-2- (1H) -on is more polar than its substrate, which is vanillin. This is due to the presence of amide groups in compounds 3,4-dihydropyrimidine-2- (1H) -on which increases the polarity of the product.

The synthesized product was analyzed using FTIR presented in Figure 3 and Table 1. FT IR functions to find out the functional groups contained in the synthesized product.

when viewed from the FT-IR spectrum, 3,4-dihydropyrimidine-2-(1H)-on product has been formed with the type of compound ethyl 4-(3-hydroxy-4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8). This product is characterized by the presence of N-H stretching functional groups in the wavenumber 3228 cm\(^{-1}\) which indicates the presence of secondary amine groups and C=O stretching at 1645 cm\(^{-1}\) which indicates the presence of NH-C = O amide groups. This is a characteristic of the functional group 3,4-dihydropyrimidine-2- (1H)-on [23]. But the product measured still contained primary amine derived from the urea substrate signal at 3462 cm\(^{-1}\). Following is the FT IR spectrum interpretation of reaction products using the KBr method.
Table 1. Interpretation of FT IR spectrum of reaction products

| Wavenumber (cm⁻¹) | Vibration modes                                      |
|-------------------|-----------------------------------------------------|
| Product           | Reported [23][24][25]                               |
| 3462              | 3514                                               | NH stretching |
| 3362              | 3360                                               | -OH stretching |
| 3228              | 3244                                               | N-H stretching (secondary amine) |
| 3108              | 3118                                               | C-H stretching (aromatics)      |
| 2949              | 2978                                               | CH₂ stretching, asymmetric CH₂ stretching |
| 1649              | 1645                                               | C=O stretching (NH-C=O amide)   |
| 1594              | 1600                                               | C-C stretching (aromatic ring)  |
| 1445              | 1475                                               | C-H bending                    |
| 1274              | 1221                                               | C-N stretching                 |
| 1026              | 1056                                               | C-O Stretching                 |
| 778               | 771                                                | C-H bending                    |

The product of the reaction in this study has characteristics with a maximum wavelength of 306.40 nm (figure 4). Research that has been reported shows that alkaloid compounds have a maximum wavelength at around 254-366 nm (Marlina, 2005) [26]. The synthesized product compound is an alkaloid compound derived from 3,4-dihydropyrimidin-2-(1H)-on. So that the wavelength is probably derived from the chromophore alkaloid compound which is a compound of 3,4-dihydropyrimidin-2-(1H)-on compounds.

Figure 4. UV-Vis spectrum of the product

In this research, the catalyst of kelubi extract was compared with the strong acid catalyst, HCl. Based on Table 2 shows that the use of HCl catalyst still has a better yield in a shorter time when compared to the catalyst extract of kelubi fruit. This can be caused by protonation using strong acids better than using fruit extracts. In addition, the use of a large amount of kelubi extract catalyst is not in line with the yield produced. The more kelubi extract used the more water in the reaction stage. Vanillin itself has a solubility of 10 g/L in water. This water is a barrier to collisions between substrate molecules so that the yield produced is lower.

The best yield of this research is 67.7% using 0,2 mL of kelubi juice with a temperature of 50°C and 180 minutes. This value is indeed still low when compared to the use of metal catalysts or strong acids. But the results of using this fruit catalyst are not too bad considering the ingredients used are eco friendly and not toxic. So that the use of the Kelubi fruit catalyst has advantages with its nature which is safe for the environment.
Table 2. The results of the synthesis of compounds 3,4-dihydropyrimidin-2-(1H)-one

| No | Catalyst                        | T (°C) | Reaction Time (min) | Yield (%) |
|----|---------------------------------|--------|---------------------|-----------|
| 1  | HCl (0.2 ml)                    | 50     | 15                  | 27.27     |
| 2  | HCl (0.2 ml)                    | 50     | 30                  | 45.45     |
| 3  | kelubi extract (10ml)           | 50     | 60                  | -         |
| 4  | kelubi extract (2ml)            | 50     | 180                 | 3.6       |
| 5  | kelubi extract (0.2ml)          | 50     | 180                 | 67.7      |

The role of acidic fruit extract is almost the same as HCl, as an acid catalyst that can donate protons. Kelubi juice extract which contains lots of ascorbic acid and anthocyanin allows for donor protons. These protons play a role in helping the formation of iminium intermediate compounds (5) [27]. These intermediates then react with ethyl acetoacetate to form product compounds ethyl 4-(3-hydroxy-4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8). Several studies reported that the iminium intermediate (5) in the Biginelli reaction can react with urea to form compounds 6 [1]. Suggestions for the mechanism of product formation with the kelubi extract catalyst are presented in scheme 1.

![Scheme 1. Proposed mechanism for Biginelli reaction to form a product with kelubi fruit as a catalyst via iminium pathway](image)

4. Conclusions
Kelubi fruit extract can be used as an acid catalyst in the synthesis of 3,4-dihydropyrimidin-2-(1H)-one. The analysis of this product is based on the FT IR spectrum which is characterized by the presence of the NH stretching function group at wavenumber 3228 cm\(^{-1}\) (secondary amine) and C=O stretching at 1645 cm\(^{-1}\) (NH-C = O amide) with RF 0.35 (eluent n-hexane: ethyl acetate 6: 4) and a maximum wave number of 306 nm. The role of the kelubi extract as an acid catalyst can donate protons. Kelubi extract which contains lots of ascorbic acid and anthocyanin allows for donor protons. These protons play a role in helping the formation of iminium intermediate compounds. When viewed from the yield and reaction time, the use of this fruit catalyst is not too bad considering the material used is eco friendly and not toxic. So that the use of the Kelubi fruit catalyst has advantages with properties that are safe for the environment. However, further research is needed to find out the optimum results for the use of this catalyst while still paying attention to the product and the rest of the environmentally friendly synthesis process.
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