Aqueous fraction of *Sapindus rarak* D.C. fruit extract mediated one-pot three component construction of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one

A H Cahyana, M C Maida and B Ardiansah

Department of Chemistry, Faculty of Mathematics and Natural Sciences (FMIPA), Universitas Indonesia, Kampus UI Depok, Depok 16424, Indonesia

Corresponding author’s e-mail: herrykim@ui.ac.id

**Abstract.** In this study, we report 3-component combination of 2-naphthol, dimedone and benzaldehyde in 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12)-one synthesis using water fraction of *Sapindus rarak* D.C. fruit extract. This extract promoted an efficient synthesis under mild reaction conditions. The compound structure was confirmed by FT-IR and Mass analysis.

1. **Introduction**

Benzoxanthene derivatives are noted to possess notable biological and pharmacological activities such as anti-inflammatory [1], antibacterial [2], and antiviral [3]. Three component reaction of aldehydes, 2-naphthol and cyclic 1,3-dicarbonyl compounds is one of highly interesting approaches for the preparation of benzoxanthene derivatives [4]. Recently, multicomponent synthesis of benzoxanthene derivatives have been performed in the presence of various catalysts such as Zr(HSO₄)₅, H₂SO₄,[6], iodine [7], ZnO [8], and pyrazinium dihydrogen sulfate [9]. However, some procedures have at least one drawback, such as long reaction times, toxic solvents or high temperature needed.

In recent years, role of green chemical-based catalysts has grown tremendously. The highlighted aspect of green chemistry is reduction in the use of harmful chemical reagents [10]. Using plant or its part as a potential biocatalyst in the synthesis of organic compounds is one of the efforts that have been conducted. Organic synthesis using natural materials generates less waste than the conventional methods [11].

*Sapindus rarak* D.C. is a plant used as a traditional detergent. The fruits, roots, and seeds contain triterpenoids, some polyphenols and saponins that act as anti-cancer, anti-bacterial, and anti-insecticides. The content of saponin content in *Sapindus rarak* D.C. fruit reaches 10–11.5 % [12]. Saponins are group of glycoside compounds that serve as a washing agent that has properties such as soap and acts as a surfactant. Surfactants are best known to dissolve the non-polar materials. That ability has established the aqueous surfactant systems to be notably popular option for organic solvents [13] or stabilizing and capping agent in nanoparticles syntheses [14]. Therefore, with interesting properties of aqueous extract of *Sapindus rarak* D.C. fruit, we investigate its performance as an eco-friendly acidic surfactant type for the synthesis of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one (figure 1).

2. **Materials and methods**

2.1. **General**

All chemicals required were obtained from Merck and used without further purified. *Sapindus rarak*
Figure 1. Multicomponent synthesis of benzo[a]xanthene using aqueous fraction of Sapindus rarak D.C. fruit extract

D.C. fruit was obtained from Banjarsari, Surakarta. Functional group analysis was done by Fourier Transform Infrared (FT-IR) on Shimadzu 8400 spectrometer with KBr background. Mass analysis was conducted on Shimadzu QP Mass Spectrometer 2010A having 70 eV ionization potential.

2.2. Preparation of Sapindus rarak D.C. fruit extract
Preparation of Sapindus rarak D.C. fruit extract (SRDFE) was carried out by maceration method. Sapindus rarak D.C. (50 g) dry powder was macerated in methanol (1:5 w/v) for 2 days. The extract was filtered and then centrifuged for 10 min. The filtrate was evaporated using a rotatory evaporator. Furthermore, this crude extract was separated by deionized water and hexane by a ratio of 1:1 (v/v). These fractions were phytochemically screened to determine secondary metabolites content such as saponins, alkaloids (Wagner test), flavonoids, steroids, terpenoids (Salkowski test), and tannins [15]. Further, aqueous fraction will be used to mediate multicomponent synthesis of a benzo[a]xanthene derivative.

2.3. Synthesis of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthene-11(12H)-one.
In 30 mL round-bottom flask, benzaldehyde (0.106 g, 1 mmol), dimedone (0.140 g, 1 mmol), 2-naphthol (0.144 g, 1 mmol) and aqueous fraction of Sapindus rarak D.C. fruit extract (5 mL) were stirred at 30 ºC. The reaction mixture was observed by Thin-Layer Chromatography (TLC) analysis using n-hexane/ethyl acetate (4:1) and spots were investigated using a UV lamp (254 and 366 nm). Once the reaction was completed, the temperature was reduced to room temperature, water was added then stirred for 3 min followed by filtering. The solid residue was isolated in crystal form from aqueous ethanol (90 %) to obtain a pure product. Sapindus rarak D.C. extract, reaction temperature and time were varied to obtain optimized protocol.

3. Results and discussion
The phytochemical screening of water and n-hexane fraction of Sapindus rarak D.C. fruit extracts revealed the presence of several secondary metabolites. Saponins were strongly observed in water fraction but not in n-hexane fraction. Alkaloids were found only in n-hexane fraction. Meanwhile, terpenoids were detected in both fractions. The results are summarized in table 1.

FT-IR spectrum of aqueous fraction of Sapindus rarak D.C. fruit extract (figure 2) showed peak at 1730 cm\(^{-1}\) due to carbonyl stretching vibration. A broad peak at 3353 cm\(^{-1}\) is associated to O-H vibration. Furthermore, peaks at 2933 and 1613 cm\(^{-1}\) are ascribed to the C-H sp and C=C vibrations, respectively. All those peaks may be attributable to the presence of saponins in the extract [16].

We report here the efficient and green approaches for the preparation of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthene-11(12H)-one using one-pot, three-component condensation of
Table 1. The results of phytochemical tests in aqueous and hexane fraction of *Sapindus rarak D.C.*

| Extract      | Water | Hexane |
|--------------|-------|--------|
| Saponin      | ++++  | -      |
| Alkaloids    | -     | +      |
| Flavonoids   | -     | -      |
| Steroids     | -     | -      |
| Terpenoids   | ++    | +      |
| Tanins       | -     | -      |

Note: + = presence, - = absence

Figure 2. FT-IR spectrum of aqueous fraction of *Sapindus rarak D.C.* fruit extract

benzaldehyde, 2-naphthol, and dimedone mediated by aqueous fraction of *Sapindus rarak D.C.* fruit extract.

In figure 3, FT-IR spectrum of organic product signified the presence of C=O band at 1604 cm⁻¹, whereas peaks at 2871 cm⁻¹ and 2966 cm⁻¹ indicated the existence of aliphatic C-H group. Meanwhile, absorption at 1371 cm⁻¹ is characteristic of C-O-C group. Mass spectra data (figure 4) shows the molecular weight of benzoxanthene derivative of 354 gmol, with molecular formula of C₂₅H₂₂O₂, fit with IUPAC name of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one.

To achieve optimum reaction conditions, we initially investigated the reaction with various catalysts, temperatures and times (catalyst: 5, 7 and 10 mL; reaction time: 15, 20, 25, and 30 min; temperature: 30, 50, 80 and 100 ºC). The best result was obtained when using 5 mL of aqueous fraction of *Sapindus rarak D.C.* fruit extract at 100 ºC for 20 min (table 2 entry 7). The optimum yield of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one obtained was 85 %. A plausible mechanism for the production of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one by the existence of saponin catalysts is proposed in figure 5. The sponins, which are acidic, could strongly dissolve the reactant species through hydrogen bond formation in aqueous medium [17]. Thus as the carbonyl group will be susceptible to other nucleophilic reactant attacks. Initially, the 2-naphthol condensation with benzaldehyde generated ortho-quinone methides (o-QMs). Then, the o-QMs with dimedone produced intermediates which were cyclized and then dehydrated to generate the corresponding of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one [7].
Figure 3. FT-IR spectrum of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one

Figure 4. Mass spectrum of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one
Table 2. Synthesis of 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen -11(12H)-one in different conditions using aqueous fraction of *Sapindus rarak* D.C.

| Entry | Fruit extract (mL) | Time (min) | Temp (ºC) | Yield (%) |
|-------|--------------------|------------|-----------|-----------|
| 1     | 5                  | 15         | 50        | 64        |
| 2     | 5                  | 20         | 50        | 72        |
| 3     | 5                  | 25         | 50        | (i) 73    |
| 4     | 5                  | 30         | 50        | 70        |
| 5     | 5                  | 20         | 30        | 64        |
| (ii)  | 6                  | 20         | 80        | (iii) 78  |
| (iv)  | 7                  | 20         | 100       | 85        |
| (v)   | 8                  | 20         | 100       | (vi) 85   |
| (vii) | 9                  | 20         | 100       | 85        |

Figure 5. Proposed mechanism in the synthesis of 9,9-dimethyl-12-phenyl -9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one

4. Conclusions
We successfully synthesized 9,9-dimethyl-12-phenyl-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one using aqueous extract of *Sapindus rarak* D.C. fruit extract containing saponins. The optimum conditions of the synthesis were obtained when 5 mL of extract used at 100 ºC for 20 min. The present research highlighted an easy work-up, low-cost, efficient and eco-friendly manner in the synthesis of biologically potent natural product derivative with excellent yield.

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