Methyl 2,5-Dihydroxy-4-(3'-methyl-2'-butenyl)benzoate

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Short Note

Methyl 2,5-Dihydroxy-4-(3′-methyl-2′-butenyl)benzoate

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Abstract: Methyl 2,5-dihydroxy-4-(3′-methyl-2′-butenyl)benzoate (**1**) was isolated from the root of *Erythrina subumbrans*. The chemical structure of **1** has been elucidated based on spectroscopy UV-Vis, HRESIMS, 1D and 2D NMR analysis.

Keywords: Methyl 2,5-dihydroxy-4-(3′-methyl-2′-butenyl)benzoate; Methyl benzoate derivative; *Erythrina subumbrans*

1. Introduction

The genus *Erythrina* (Euphorbiaceae) comprises more than 100 species that are widely distributed in tropical and subtropical regions. The evergreen plants of *Erythrina* occur in almost every part of Indonesia, from Sumatra to Irian and the plants is commonly known as 'dadap'. Many of these species are used indigenously as traditional medicines to treat various diseases, such as infection, cough, malaria, inflammation, and asthma. This genus has been shown to produce a number of phenolic compounds, particularly alkaloids [1], flavonoids [2,3], pterocarpans [4,5] and stilbenoids [6]. In continuation of our research into the phenolic compound in this medicinal plant, we report the isolation of methyl 2,5-dihydroxy-4-(3′-methyl-2′-butenyl)benzoate (**1**) from the methanol extract of the the root of *Erythrina subumbrans*. The chemical structure of compound **1** was established by UV, HRESIMS, 1D and 2D NMR, as well as by comparison with those related compounds previously reported. The antioxidant activity against DPPH radical scavenging of the isolated compound **1** is also briefly described.

2. Result and Discussion

Extraction of the dried milled of roots of *E. subumbrans* (1.5 kg) was carried out using methanol, and then methanol extract was partitioned with *n*-hexane and ethyl acetate. The ethyl acetate extract (18 g) was separated by vacuum liquid chromatography on silica gel and radial chromatography yielded methyl 2,5-dihydroxy-4-(3′-methyl-2′-butenyl) benzoate **1** (Figure 1).

Methyl 2,5-dihydroxy-4-(3′-methyl-2′-butenyl)benzoate (**1**) was isolated as white solid. The UV spectrum exhibited absorption maxima λ_{maks} 224 and 287 typical for a 4-methyl benzoate chromophore [7]. The HRESIMS spectrum showed a quasimolecular ion $[M - H]^-$ at m/z 235.0971 (calcd. 235.0970), which correspondend to the molecular formula of $C_{13}H_{15}O_4$. The ^{1}H-NMR (Table 1) spectrum of **1**, the presence of two singlet aromatic proton signals at δ_H 7.56 (1H, *s*, H-6) and 6.39 (1H, *s*, H-3) suggest that compound **1** is typical for a methyl benzoate with three substituents [8]. In the ^{13}C-NMR spectrum (Table 1), the results for **1** showed 13 carbon signals consistent for methyl isoprenylated benzoate structure, and two carbon signals at δ_C 52.0 and 170.4 were assigned to a methoxyl and carbonyl carbon from methyl benzoate structure. These spectroscopic data, therefore, suggested that **1** is a methyl benzoate containing an isoprenyl (3′-methyl-2′-butenyl) side chain.

Furthermore, the presence of other two oxyaryl signals (δδ$_C$ 160.9 and 162.1) indicated that the methyl benzoate has two hydroxyl groups. The side chain was deduced to be an isoprenyl group from the observation in the ^{1}H-NMR spectrum (Table 1) of two methyl singlets (δ_H 1.76 and 1.77), one methylene signal (δ_H 3.27), and one methin vinyl signal (δ_H 5.28). The presence of a chelated –OH group at δ_H 10.79 gave the position of hydroxyl at C-2. The presence of long range correlations in the HMBC spectrum between the proton signal δ_H 10.79 with two quartenery carbon signals at δ_C 105.4 (C-1), 162.1 (C-2) and one methyne carbon at δ_C 103,4 (C-4) confirmed the -OH group (δ_H 10.79) attached at C-2. In the aromatic region of ^{1}H-NMR spectrum, two singlet signals at δ_H 6.39 and 7.56 suggested that the position protons are found at H-3 and H-6. The presence of long range correlations in the HMBC spectrum of **1** between the proton signal aromatic at H-3 (δ_H 6.39) with four quarternary carbon signals at δ_C 105.4 (C-1), 162.1 (C-2), 119.2 (C-4), and 160.9 (C-5) unambiguously placed the isoprenyl at C-4 and hydroxyl groups at C-2 and C-5. The placement of isoprenyl group at C-4 suggested the correlation methylene signal (δ_H 3.27) with three quarternary carbon signals at δ_C 160.9 (C-5), 119.2 (C-4), 135.0 (C-3′), and two tertiery carbon signals at δ_C 103.4 (C-3), 121.6 (C-2′). Therefore, compound **1**, was elucidated as methyl 2,5-dihydroxy-4-(3′-methyl-2′-butenyl)benzoate. Other HMBC correlations consistent with the structure **1** are shown in Table 1 and Figure 2. To our knowledge, compound **1** was the first example of methyl benzoate derivative in the genus *Erythrina* with an isoprenyl side chain.

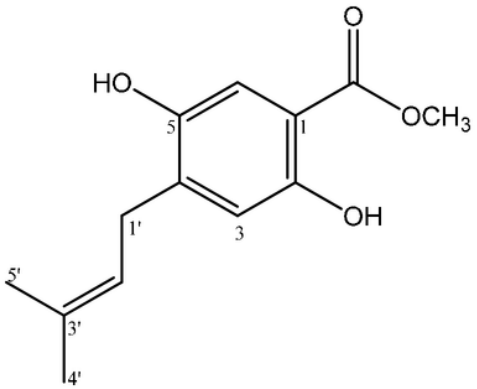

Figure 1. Structure of methyl 2,5-dihydroxy-4-(3′-methyl-2′-butenyl)benzoate (**1**).

Table 1. NMR spectroscopic data of methyl 2,5-dihydroxy-4-(3′-methyl-2′-butenyl)benzoate in $CDCl_3$.

No. C	δ_H ppm (mult, *J* Hz)	δ_C ppm	HMBC
1	-	105.4	-
2	-	162.1	-
3	6.39 (s, 1H)	103.4	C-1, C-2, C-4, C-5
4	-	119.2	-
5	-	160.9	-
6	7.56 (s, 1H)	131.1	C-2, C-4, C=O
1′	3.27 (d, 7.0, 2H)	28.9	C-3, C-4, C-5, C-2′, C-3′
2′	5.28 (tm, 7.5, 1H)	121.6	C-4′, C-5′
3′	-	135.0	-
4′	1.77 (s, 3H)	25.8	C-2′, C-3′, C-5′
5′	1.76 (s, 3H)	17.9	C-2′, C-3′, C-4′
C=O	-	170.4	-
2-OH	10.79 (s, 1H)	-	C-1, C-2, C-3
OCH_3	3.91 (s, 3H)	52.0	C=O

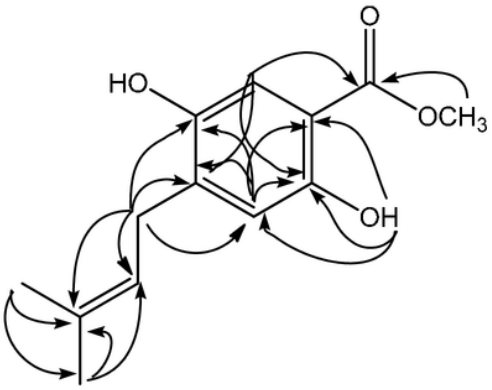

Figure 2. Selected HMBC correlations for compound **1**.

On antioxidant evaluation against DPPH radical scavenging, compound **1** exhibited IC_{50} values of 266.48 µg/mL. That cytotoxic data suggested that compound **1** has moderate activity.

3. Material and Methods

3.1. General Information

NMR spectra were recorded on an Agilent 500 spectrometer (Santa Clara, CA, USA) in $CDCl_3$ at 500 (^{1}H) and 125 (^{13}C) MHz using TMS as the internal standard. The mass spectra was recorded using a Waters LCT Premier XE (Santa Clara, CA, USA). The UV was measured with a Shimadzu 1800 spectrophotometer (Kyoto, Japan). Vacuum-liquid chromatography (VLC) and radial chromatography were carried out using Si gel 60 GF_{254} and Si gel 60 PF_{254}, for TLC analysis, and pre-coated silica gel plates (Merck, Darmstadt, Germany, Kieselgel 60 GF_{254}, 0,25 mm thickness) were used.

3.2. Plant Material

Samples of roots of *E. subumbrans* were collected in December 2014 from Botanical Garden, Pasuruan, Indonesia, and the specimen was deposited at the herbarium. The roots were cleaned, air dried under the shade, cut into small pieces and milled.

3.3. Extraction and Isolation

The dried roots of *E. subumbrans* (1.5 kg) were macerated in methanol at room temperature twice, and the methanol extract was evaporated under reduced pressure to give a dark brown residue (90 g). The crude extract in methanol (90 g) was partitioned first with *n*-hexane. The methanol layer was added with water (5% *v*/*v*) to increase the polarity and then partitioned with ethyl acetate. The ethyl acetate extract (18 g) was separated by vacuum liquid chromatography on silica gel. Elution with *n*-hexane–ethyl acetate by gradient amount of ethyl acetate (90:10, 80:20; 70:30; 50:50 and 20:80) to give five major fractions A–E. TLC on fraction B (460 mg) using eluent *n*-hexane–chloroform 1:1, showed two major spots. Purification of this fraction using planar radial chromatography, and eluting with *n* hexane–chloroform (from 2:8 to 1:1) yielded compound **1** (48 mg).

3.4. DPPH Radical Scavenging

The antioxidant assay of compound **1** against DPPH (2,2-diphenyl-1-picrihidrazil) radical was measured by UV spectrometer at λ 517 nm as described previously [9,10]. The inhibition percentage (%) of radical scavenging activity was calculated using the following equation:

$$\text{Inhibition}\,(\%) = (A_o - A_s/A_o) \times 100 \quad (1)$$

where A_o is the absorbance of the control reaction (containing all reagents except the test compound), and A_s is the absorbance of the test compound.

Supplementary Materials: ^{1}H-NMR, ^{13}C-NMR and HRESIMS spectra are reported in the supplementary materials as Figure S1–S5 together with structure refinement parameters as Table S1. They and the molfiles can be found at http://www.mdpi.com/1422-8599/2016/2/M892.

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Author Contributions: Mulyadi Tanjung designed the whole experiment and contributed to the manuscript. Tjitjik Srie Tjahjandarie researched data and wrote the manuscript, Ratih Dewi Saputri analyzed the NMR and HRESIMS spectra. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare no conflict of interest

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