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Phthalate Derivative from the Non-Polar Fraction of Andaliman (*Zathoxylum acanthopodium* DC.) Stem Wood from North Sumatra

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Abstract

Andaliman (*Z. acanthopodium* DC.), a plant belonging to the *Zanthoxylum* genus, is widely found in North Sumatra. *Z. acanthopodium* DC. has been traditionally used by local people to treat various diseases. Several secondary metabolites have been reported from the *Zanthoxylum* genus, including coumarins, flavonoids, lignans, terpenoids, steroids, amides, alkaloids, and phthalate derivatives. In this study, a phthalate derivative compound has been successfully isolated from the non-polar fraction of the stem wood of *Z. acanthopodium* DC., which was identified as di-(2-ethylhexyl) phthalate according to IR and NMR spectroscopic analyses.

Keywords: Andaliman, di-(2-ethylhexyl) phthalate, *Zanthoxylum*, *Zanthoxylum acanthopodium* DC

1 Introduction

Z. acanthopodium DC., a flowering plant from the *Zanthoxylum* genus, is commonly found in North Sumatra, Indonesia. In addition to the North Sumatra highlands, the habitats of this plant cover a wider region, including Southwestern China, India, Nepal, Vietnam, Malaysia, and Thailand [1]. Locally known as Andaliman or merica Batak, this plant is widely used to add spicy flavor and characteristic aroma to Batak cuisine [1]. Aside from its utility as a seasoning, *Z. acanthopodium* DC. has been traditionally used as folk medicine to treat various ailments [1,2]. The medical benefits of this plant has been attributed to its diverse biological activities, including anti-inflammatory [3,4], anticancer [5,6], analgesic [7], antibacterial [8], antifungal [9], and wound healing activities [10].

Various secondary metabolites have been isolated from the *Zanthoxylum* genus, including alkaloids [11], lignans [12], coumarins [13], amides [14], steroids [15], terpenoids [16], and phthalate derivatives [9]. Phthalate derivatives, in particular, are abundant in many plants and have been isolated from species like *Vicia villosa* Roth [17], *Sonneratia alba* [18], *Aloe vera* [19], *Phyllanthus muellerianus* [20], and *Laminaria japonica* [21]. Furthermore, these phthalate derivatives have been reported to exhibit antibacterial activity [22], antileukaemic, and antimutagenic effects [19]. In this study, we isolated a phthalate derivative from the non-polar fraction of the stem wood of *Z. acanthopodium* DC. from North Sumatra.

2 Methods

2.1 *Plant Material*

The stem wood of *Z. acanthopodium* DC. was collected from Toba Samosir, North Sumatera, Indonesia, in 2018 and identified in the Herbarium Bogoriense, National Research and Innovation Agency, Cibinong, West Java.

2.2 *Extraction and Isolation*

The stem wood of *Z. acanthopodium* DC. (3 kg) was macerated in MeOH for 3x24 hours at room temperature, and the filtered extract was concentrated under reduced pressure to give the MeOH extract (20.9 g). The MeOH extract was then partitioned with *n*-hexane, $CHCl_3$, and EtOAc successively to yield an *n*-hexane-soluble fraction (3.4 g), a $CHCl_3$-soluble fraction (5.9 g), and an EtOAc-soluble fraction (6.4 g), respectively. The *n*-hexane extract was fractionated by vacuum liquid chromatography over silica gel (70-230 mesh) with a step gradient of *n*-hexane–EtOAc (10:0, 9.5:0.5, 9:1, 0:10) as

eluent to afford four combined fractions (A–D) following the monitored using TLC on aluminium plates coated with silica gel GF_{254} and detected by short wavelength ultraviolet light (254 nm). Fraction A (977.7 mg) was subsequently subjected to vacuum liquid chromatography eluting with *n*-hexane–EtOAc (9.75:0.25 and 0:10) to give ten fractions, which were combined into three fractions (A1–A3). Fraction A1 (768 mg) was further chromatographed on a Si gel column with *n*-hexane–diisopropyl ether (9.5:0.5) to obtain compound **1** (466.1 mg).

2.3 *Compound Characterization*

IR spectrum was recorded using the FTIR spectrometer Shimadzu 8400. ^{1}H NMR spectrum was recorded on an NMR Agilent DD2 500 MHz spectrometer, and chemical shifts are reported in parts per million (ppm).

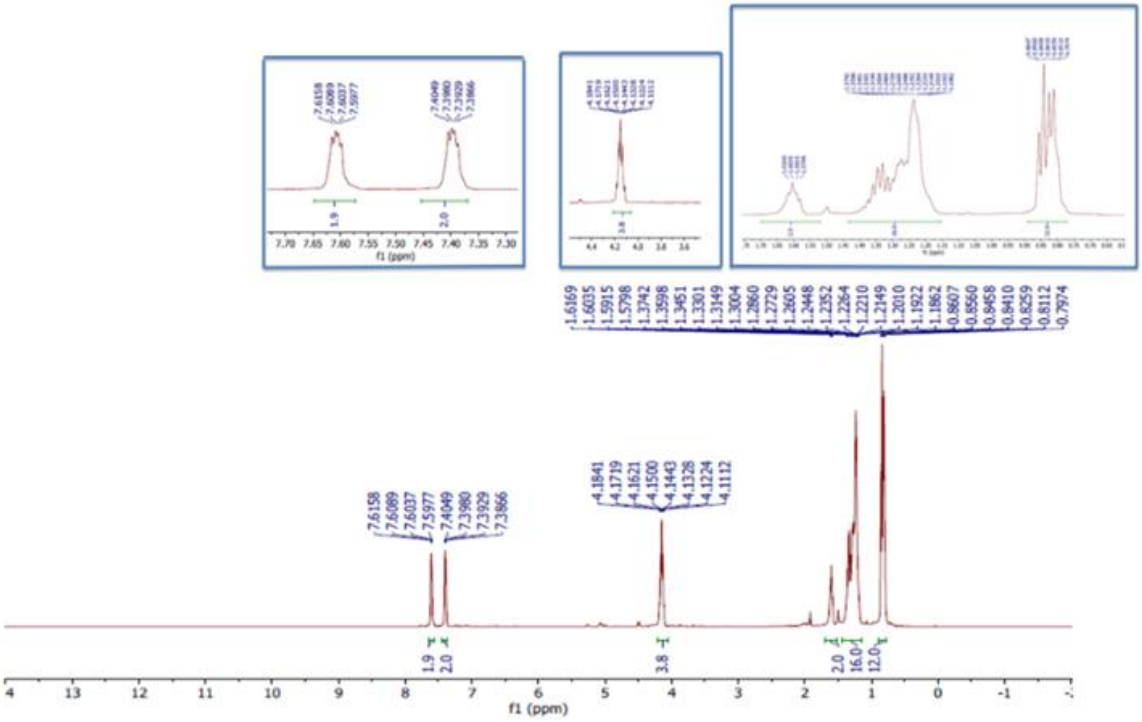
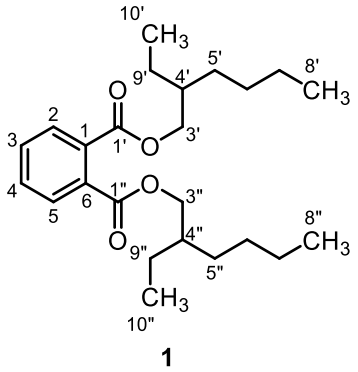


Figure 1. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **1**.

3 Results and Discussion

Compound **1** was isolated as a yellow oily liquid. The IR spectrum showed absorption bands for the alkyl group (C–H stretching of sp^3 carbons at 2891 cm^{-1}), ester (C=O stretching at 1728 cm^{-1} and C–O stretching at 1274 and 1136 cm^{-1}), and aromatic benzene ring (C=C stretching at 1593 and 1464 cm^{-1}).

The ^{1}H NMR spectrum (Figure 1) of **1** showed the presence of multiplets corresponding to four methyl protons at δ_H 0.79-0.86 ppm eight methylene protons at δ_H 1.19-1.37 ppm, and two methine protons at δ_H 1,58-1.62 ppm. A multiplet integrating to four protons was observed at a downfield region of δ_H 4.11-4.18 ppm, indicating a pair of oxygenated methylene protons (H3' and H3"). The existence of two sets of double of doublets with integration of two each at δ_H 7.39 ppm (J = 3, 6 Hz, H3, H4) and 7.60 ppm (J = 3, 6 Hz, H2, H5) further confirmed a symmetrical *ortho*-disubstituted benzene, suggesting a phthalate derivative. By comparison of ^{1}H NMR data with those reported in the literature [23,24], compound **1** was identified as di-(2-ethylhexyl) phthalate (Figure 2). Although this compound is known, di-(2-ethylhexyl) phthalate was isolated from *Z. acanthpodium* DC for the first time.



1

Figure 2. Structure of compound **1** (di-(2-ethylhexyl) phthalate) isolated from the stem wood of *Z. acanthopodium* DC.

4 Conclusion

A phthalate derivative, di-(2-ethylhexyl) phthalate, has been successfully isolated from the *n*-hexane extract of the stem wood of *Z. acanthpodium* DC. as a yellow oil. This is the first report of the isolation of this compound from *Z. acanthpodium* DC.

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