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A Benzoate of *Synsepalum Dulcificum*

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ABSTRACT

*A benzoate, ethyl 4-hydroxybenzoate (**1**) was isolated from the stems of Synsepalum dulcificum Daniell (Sapotaceae). The structure of the benzoate was elucidated by chemical and physical evidence.*

Keywords

Synsepalum dulcificum, Sapotaceae, Stems, Benzoate.

Introduction

Synsepalum dulcificum Daniell (Sapotaceae) is an evergreen shrub native of tropical West Africa; and its fruit, red berries, have the property of remarkably altering the sour taste into sweet taste [1]. This explains why that the berry has been called "miracle fruit or mysterious fruit". In the course of screening for chemically novel agents from plants, *S. dulcificum* was chosen for further phytochemical investigation [2-5]. In the course of screening for biologically and chemically novel agents from Formosan Sapotaceous plants [6,7], *S. dulcificum* was chosen for further phytochemical investigation. In continuation of some studies of chemotaxonomy and biologically active metabolites from this plant, a methanol extraction of the stems of *S. dulcificum* afforded 7 compounds, including ethyl 4-hydroxybenzoate (**1**), propane-1,2,3-triol (**2**), 2,5-dimethoxyphenol (**3**), 3,4,5-trimethoxybenzoic acid (**4**), nicotinic acid (**5**), β-sitosterol (**6**) and stigmasterol (**7**) [8]. In this paper, we report the isolation and structural elucidation of this benzoate (**1**).

Ethyl 4-hydroxybenzoate (**1**), obtained as a white powder, established by the molecular formula $C_9H_{10}O_3$ by HR-EIMS at *m/z* $[M + Na]^+$ 189.0522 (calcd for $C_9H_{10}O_3Na$, 189.0528). Two IR bands at ν_{max} 3300 and 1670 cm^{-1} and a signal appearing at δ 168.1 in the ^{13}C NMR spectrum suggested that hydroxyl groups and a ester group might be present. The ^1H NMR spectrum revealed an AA′BB′ pattern at δ 7.36 (2H, d, J = 9.0), and 6.84 (2H, d, J = 9.0) for H-2,6′ and H-3,5′, one methylene protons at δ 4.01 (2H, q, J = 7.2) for H-1′, one methyl protons at δ 1.39 (3H, t, J = 7.2) for H-2′, respectively. ^{13}C NMR and DEPT experiments on **1** showed 9 resonance lines consisting of one methyl, one methylene, four methines and three quaternary carbons (including one carbonyl signal at δ 168.1).

The mass, UV, IR and ^1H NMR data suggested that **1** is a type of benzoate and that the position of hydroxyl group should be located on the skeleton. The sequential correlations of the NOESY spectrum were successfully established as shown in Figure 1. Thus, the structure of this compound was named to be ethyl 4-hydroxybenzoate (**1**), which was further confirmed by HMBC experiments (Table 1).

Table 1: NMR data of **1** in $CDCl_3$ (δ in ppm, *J* in Hz, 400 MHz for ^1H NMR, and 100 MHz for ^{13}C NMR).

Position	δ_C	δ_H	*mult., J (Hz)*	*HMBC ($^1H \rightarrow {}^{13}C$)*
1	130.8	–	–	–
2	121.9	7.36	d, 9.0	C-1, C-3(C-5), C-4
3	114.8	6.84	d, 9.0	C-1, C-2(C-6), C-4
4	155.9	–	–	–
5	114.8	6.84	d, 9.0	C-1, C-2(C-6), C-4
6	121.9	7.36	d, 9.0	C-1, C-3(C-5), C-4
7	168.1	–	–	–
1′	63.7	4.01	q, 7.2	C-2′
2′	14.8	1.39	t, 7.2	C-1′

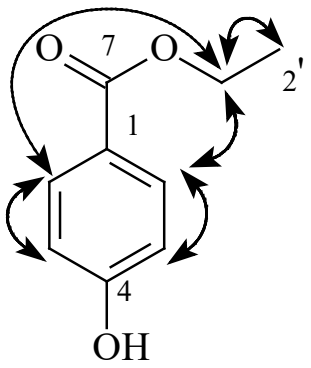

Figure 1: NOESY correlations of **1**.

Experimental

General

UV spectra were obtained in CH_3CN, IR spectra were measured on a Hitachi 260-30 spectrophotometer. ^1H NMR (400 MHz), ^{13}C NMR (100 MHz), HETCOR, HMBC, COSY, NOESY, and DEPT spectra were obtained on a Varian (Unity Plus) NMR spectrometer. Low-resolution ESI-MS spectra were obtained on an API 3000 (Applied Biosystems) and high-resolution ESI-MS spectra on a Bruker Daltonics APEX II 30e spectrometer. Silica gel 60 (Merck, 70~230 mesh, 230~400 mesh) was used for column chromatography. Precoated Silica gel plates (Merck, Kieselgel 60 F-254), 0.20 mm and 0.50 mm, were used for analytical TLC and preparative TLC, respectively, visualized with 50% H_2SO_4.

Plant Material

The specimen of the fruits of *S. dulcificum* was collected from Kaohsiung County, Taiwan, in October 2007. A voucher specimen was identified by Dr Fu-Yuan Lu (Department of Forestry and Natural Resources College of Agriculture, National Chiayi University) and was deposited in the School of Medical and Health Science, Fooyin University, Kaohsiung County, Taiwan.

Extraction and Isolation

The stems (6.14 kg) of *S. dulcificum* were extracted repeatedly with MeOH at room temperature for 24–48 h. The MeOH extract was dried and evaporated to leave a viscous residue (425.8 g). The residue was placed on a silica gel column and eluted with CH_2Cl_2 gradually enriched with MeOH to produce 4 fractions. Fraction 1 (6.38 g) was subjected to silica gel CC by eluted with *n*-hexane–EtOAc (5:1) to obtain β-sitosterol (**6**) (12 mg) and stigmasterol (**7**) (8 mg), respectively. Fraction 2 (4.15 g) eluted with CH_2Cl_2–MeOH (80:1) was further separated using silica gel CC (*n*-hexane–acetone, 2:1) to yield 3,4,5-trimethoxybenzoic acid (**4**) (3 mg). Fraction 3 (8.61 g) eluted with CH_2Cl_2–MeOH (50:1) was further purified by silica gel CC using the same solvent system and preparative TLC (CH_2Cl_2–MeOH, 10:1) to give propane-1,2,3-triol (**2**) (8 mg), 2,5-dimethoxyphenol (**3**) (5 mg) and nicotinic acid (**5**) (6 mg). Fraction 4 (7.33 g) eluted with CH_2Cl_2–MeOH (40:1) was further purified by silica gel CC using the same solvent system and preparative TLC (CH_2Cl_2–MeOH, 15:1) to give ethyl 4-hydroxybenzoate (**1**) (4 mg).

Ethyl 4-hydroxybenzoate (1). White powder. UV λmax (MeCN, log ε) 213 (2.75), 253 (3.53), 273 (2.42) nm. IR (vmax, cm-1): 3300 (OH), 1670 (C=O). ESI-MS m/z 189 [M+Na]+; HR-ESI-MS m/z 189.0522 [M+Na]+ (calcd for C9H10O3Na, 189.0528). 1H and 13C NMR data, see Table 1.

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