

Furan Derivatives and Amides from *Elaeocarpus apiculatus*

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Abstract: The first phytochemical study of *Elaeocarpus apiculatus* led to the isolation of five compounds, including two furan derivatives (**1** and **2**) and three amides (**3–5**). Among them, compound **1** was a new furan derivative, and compounds **2–5** were discovered from the genus *Elaeocarpus* for the first time. The characterization of these compounds was achieved by HRMS, UV, IR and NMR data. Compounds **1**, **3** and **4** showed weak nitric oxide (NO) inhibitory effects. A potential biogenetic pathway for the formation of **1** was proposed.

Keywords: *Elaeocarpus apiculatus*; Elaeocarpaceae; furan derivative; amide. © 2022 ACG Publications. All rights reserved.

1. Plant Source

The leaves of *Elaeocarpus apiculatus* were collected in June 2019 from Zhejiang Province, People's Republic of China, and was identified by one of the authors (S. Yao). A voucher specimen (accession number: DY190633) was deposited in the Herbarium of Zhejiang University (HZU).

2. Previous Studies

Elaeocarpus apiculatus (Elaeocarpaceae) is a common ornamental tree mainly distributed in south China [1]. However, no phytochemical studies on this plant have been reported.

3. Present Study

In the present investigation, five compounds (Figure 1) including a new furan derivative were isolated from *Elaeocarpus apiculatus*. The air-dried leaves of *E. apiculatus* (3 kg) were percolated 95% ethanol (15 L) to give an extract (195 g), which was dissolved in water and partitioned with ethyl acetate (EtOAc). The EtOAc portion was separated *via* macroporous resin D101 column chromatography (CC) and then separated *via* silica gel CC (petroleum ether/CH₂Cl₂, 20:1 → 0:1) to give five fractions (A–E). Compounds **3** (11 mg), **4** (10 mg) and **5** (8 mg) were isolated from fraction C by HPLC, while Compounds **1** (2 mg) and **2** (6 mg) were isolated from fraction D by repeated silica gel CC.

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Elapifuran A (1): colorless oil, $[\alpha]_D^{25}$ 0 (*c* 0.1, MeCN); UV (MeCN) λ_{\max} (log ϵ) 190 (3.61), 278 (2.98) nm; IR (KBr) ν_{\max} 3441, 2924, 2853, 1719, 1670, 1517, 1465, 1025, 769 cm^{-1} ; ^1H and ^{13}C NMR data, see Table 1; HRESIMS m/z 257.0415 $[\text{M} + \text{Na}]^+$ (calcd for $\text{C}_{12}\text{H}_{10}\text{O}_5\text{Na}^+$, 257.0420).

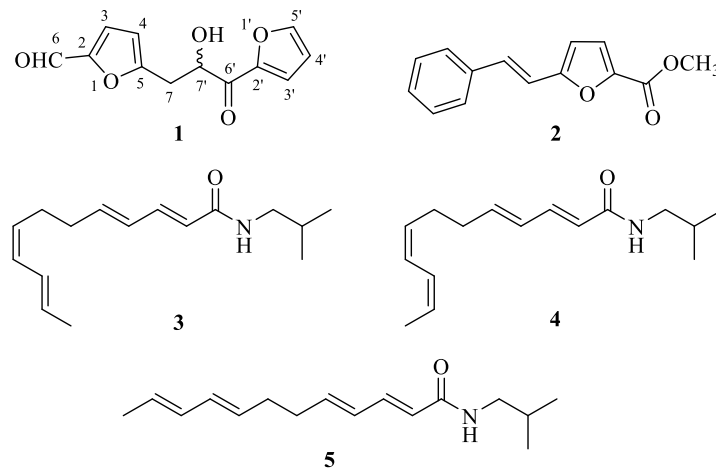


Figure 1. Structures of compounds **1–5** isolated from *E. apiculatus*

Elapifuran A (1) was obtained as colorless oil. The molecular formula was determined as $\text{C}_{12}\text{H}_{10}\text{O}_5$ by HR-ESI-MS ion at m/z 257.0415 $[\text{M} + \text{Na}]^+$ (calcd for $\text{C}_{12}\text{H}_{10}\text{O}_5\text{Na}^+$, 257.0420). In the IR spectrum, absorption bands at 3441 cm^{-1} (OH group) and 1719 cm^{-1} (carbonyl group) were observed. The ^1H NMR data of **1** (Table 1) showed an aldehyde group [δ_{H} 9.54 (1H, s)], five aromatic proton signals [δ_{H} 7.68 (1H, brs), 7.40 (1H, d, $J = 3.6$ Hz), 7.17 (1H, d, $J = 3.5$ Hz), 6.64 (1H, dd, $J = 3.6, 1.5$ Hz) and 6.41 (1H, d, $J = 3.5$ Hz)], an oxygenated methine [δ_{H} 5.17 (1H, m)] and a free hydroxyl group [δ_{H} 3.69 (1H, d, $J = 6.6$ Hz)]. Total twelve carbon resonances were resolved in the ^{13}C NMR spectrum and were further classified by HSQC as one conjugated aldehyde (δ_{C} 177.1), one conjugated ketocarbonyl (δ_{C} 188.2), eight aromatic carbons (δ_{C} 158.1, 152.2, 149.9, 147.7, 123.1, 119.8, 113.0 and 111.3), oxygenated methine (δ_{C} 71.5) and sp^3 methylene (δ_{C} 34.6). The above evidences indicated that compound **1** should be a furan derivative [2,3].

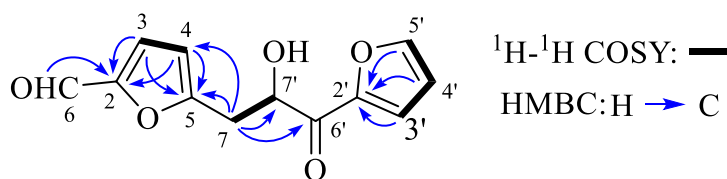
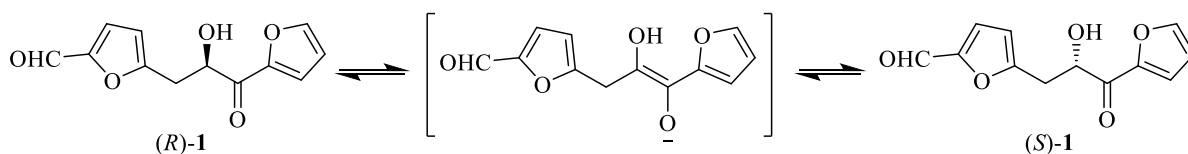
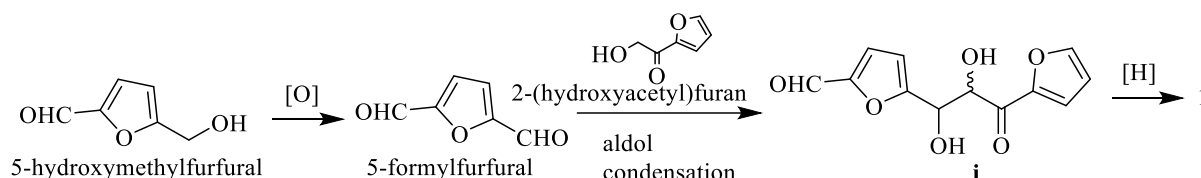


Figure 2. Key ^1H – ^1H COSY and HMBC correlations of compound **1**

In the ^1H – ^1H COSY spectrum, the correlations established coupling relationships of H-3/H-4, H₂-7/H-7' and H-3'/H-4'/H-5'. The linkages of these subunits and other functionalities were deduced by the HMBC signals. The HMBC correlations of H-3 and H-4/C-2 and C-5; H-6/C-2; H₂-7/C-4 and C-5 established a 2,5-disubstituted furan ring with an aldehyde group (C-6) at C-2 and a sp^3 methylene (C-7) at C-5. The HMBC correlations from H-3', H-4' and H-5' to C-2', together with the severely up-field shifted ketocarbonyl carbon signal (δ_{C} 188.2, C-6') indicated the existence of a monosubstituted furan ring with a ketocarbonyl group at C-2'. Finally, the HMBC correlations from H₂-7 to C-6' and C-7' generated the whole planar structure of **1**.

Furan derivatives and amides from *Elaeocarpus apiculatus***Figure 3.** The tautomerism of (*R*)-**1** and (*S*)-**1**

Compound **1** was determined to be a racemate on the basis of its optical rotation being almost zero and no Cotton effects in its ECD spectrum. However, chiral-phase separation of **1** using various conditions failed, probably due to the tautomerism of (*R*)-**1** and (*S*)-**1** (Figure 3).

**Figure 4.** Proposed biosynthetic pathway of compound **1**

A potential biosynthetic pathway of was proposed for **1** (Figure 4). Briefly, **1** might be originated from 5-hydroxymethylfurfural [4], which could be converted to 5-formylfurfural via oxidation. Then, aldol condensation between 5-formylfurfural and 2-(hydroxyacetyl)furan could afford intermediate **i**. Finally, this intermediate would undergo reduction to yield compound **1**.

Table 1. ^1H (400 MHz) and ^{13}C (100 MHz) NMR data for compound **1** (δ in ppm, J in Hz) in CD_3Cl_3

No	δ_{H}	δ_{C}	no.	δ_{H}	δ_{C}
2		152.2	2'		149.9
3	7.17, d (3.5)	123.1	3'	7.40, d (3.6)	119.8
4	6.41, d (3.5)	111.3	4'	6.64, dd (3.6, 1.5)	113.0
5		158.1	5'	7.68, brs	147.7
6	9.54, s	177.1	6'		188.2
7a	3.39, dd (15.3, 4.0)	34.6	7'	5.17, m	71.5
7b	3.11, dd (15.3, 7.9)		7'-OH	3.69, d (6.6)	

The known compounds were identified as 5-styrylfuran-2-carboxylic acid methyl ester (**2**) [5], (*2E,4E,8Z,10E*)-*N*-isobutyldodeca-2,4,8,10-tetraenamide (**3**) [6], (*2E,4E,8Z,10Z*)-*N*-isobutyldodeca-2,4,8,10-tetraenamide (**4**) [7] and (*2E,4E,8E,10E*)-*N*-isobutyldodeca-2,4,8,10-tetraenamide (**5**) [6], by comparison with the published data.

The inhibitory effects of compounds **1–5** on nitric oxide production induced by lipopolysaccharide were evaluated using a Griess assay [8], and quercetin ($\text{IC}_{50} = 16.6 \pm 1.2 \mu\text{M}$) was used as a positive control. Compounds **1**, **3** and **4** showed weak inhibitory activity with IC_{50} values of 54.6 ± 8.9 , 38.6 ± 4.4 and $44.6 \pm 5.6 \mu\text{M}$, respectively, without cytotoxicity. Other two compounds showed no obvious inhibitory effects.

The *Elaeocarpus* is characterized by alkaloids, glycosides, flavonoids, triterpenes, tannins and fatty acids, etc [9]. This is the first phytochemical study of *Elaeocarpus apiculatus*, from which two furan derivatives (**1** and **2**) and three amides (**3–5**) were isolated. All compounds were isolated from this genus for the first time. The current study could enrich the structural diversity of *Elaeocarpus* metabolites.

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Supporting Information

Supporting Information accompanies this paper on <http://www.acgpubs.org/journal/records-of-natural-products>

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